Application of Controlled Polymerisation Techniques to the Synthesis of Polymers for the Biomedical Industry

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A thesis submitted for the degree of Doctor of Philosophy

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August 2000

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I wish to thank Dave Haddleton my primary supervisor who has been of great help throughout my time at Warwick. I would also like to thank my industrial supervisors Sean Willis and Andy Muir and Biocompatibles for funding.

My praise goes to the Post-Docs that have come and gone during my time in the Haddleton empire, in particular Dax Kukulj and Stefan Bon deserve a special mention for passing on their experience and also for having great patience.

There are many people that deserve thanks for offering me advice and assisting me in times of need and it is impossible to list them all here by name. Therefore a big thank you to everyone who has been part of the polymer group over the past few years and I am sure I will remember you all for one reason or another in times to come.

On a more personal note I would like to thank Alex and Sarah for all those little 'favours' they have done for me and I promise I won't ask you to help me move any more! Thanks to Dr Simon Collins MD for telling me what Pseudomonas aeruginosa and the like really are.

I would also like to thank Andrea who has been by my side for almost as long as I can remember and has given me much joy and provided comfort, encouragement and advice during times of need.

That just leaves me to thank my family for being so patient with me and I promise I have missed you all as much as you have missed me.

V Declaration

The work described in this thesis is original research that was carried out by the author in the Department of Chemistry, University of Warwick. Results that are not those of the author are acknowledged and referenced in the usual manner throughout the text. It is the belief of the author that none of the material contained herein has been previously submitted for a degree or diploma from any university or institute of education.

Signed  Date 17.10.2000

VI Abstract

This thesis is a feasibility study into the application of controlled polymerisation techniques to the production of polymers for use in the biomedical industry and was funded by Biocompatibles Ltd. UK. The focus has been polymerisation of functional methacrylates of interest to contact lens design and in particular the synthesis of polymers with terminal unsaturation (macromonomers). Monomers investigated include tris(trimethylsiloxy)-3-methacryloxy propylsilane (TRIS), 2-(methacryloxyethyl)-2'-(trimethylammoniumethyl)phosphate (HEMA-PC), 2-(2'-hydroxy-5'-methacrylyloxyethylphenyl)-2H-benzotriazole (NORBLOC) and 2-(2-hydroxy-3-*tert*-butyl-5-vinylphenyl)-5-chloro-2H-benzotriazole (UVAM). The polymerisation techniques investigated are conventional chain transfer using mercaptans, catalytic chain transfer polymerisation and transition metal mediated living radical polymersiation (TMM-LRP). The application of these polymerisation techniques to the monomers discussed has been successful but not without certain difficulties. The production of macromonomers by the first two methods is relatively well documented however there are no reports of macromonomer production via TMM-LRP and in this thesis several methods of end group functionalisation have been demonstrated.

VII Abbreviations

Λ	Molecular weight distribution
ν	Kinetic chain length
AA	Acrylic acid
AEMA	2-Aminoethyl methacrylate hydrochloride
AIBN	2,2'-azo-bis-isobutyronitrile
$[Al(OiPr)_3]$	Aluminium tri-*iso*-propoxide
AN	Polar acrylonitrile copolymer mould
ATP	Atom transfer polymerisation
ATRA	Atom transfer radical addition
ATRP	Atom transfer radical polymerisation
n-BMA	*n*-Butyl methacrylate
BPO	Dibenzoylperoxide
CCT	Catalytic chain transfer
CCTA	Catalytic chain transfer agent
CCTP	Catalytic chain transfer polymerisation
CLD	Chain length dependent
CoBF	[Bis{μ-[(2,3-butanedione dioximato(2-)O:O']} tetrafluorodiborato(2-)-*N*,*N*',*N*'',*N*'''] cobalt or Cobaloxime boron fluoride or Bis(boron difluorodimethlygloximato) cobaltate(II)
CoPhBF	[Bis{μ-[diphenylethanedione dioximate(2-)O:O']}tetrafluorodiborato(2-)-*N*,*N*',*N*'',*N*''']cobalt
Cs	Chain transfer constant
CSIRO	Commonwealth scientific and industrial research organisation
CTA	Chain transfer agent
DK	Oxygen permeability
DK/L	Oxygen transmissibility
DMA	*N*,*N*-Dimethylacrylamide
DMF	Dimethylformamide
DMSO	Dimethylsulphoxide
DP	Degree of polymerisation
DP_n	Number average degree of polymerisation

DP_{n0}	Degree of polymerisation in absence of chain transfer agent
DPPH	1,1-diphenyl-2-picrylhydrazyl
DP_w	Weight average degree of polymerisation
DRI	Differential refractive index
EDCI	1-(3-Dimethylaminopropyl)-3-ethyl-carbodiimmide hydrochloride
EWC	Equilibrium water content
f	Efficiency factor
f_a & f_b	Mole fraction of a or b in monomer feed
F_A & F_B	Mole fraction of A or B in polymer
FDA	Food and drug administration
GM	Glycerol methacrylate
GPC	Gel permeation chromatography
HEMA	2-Hydroxyethyl methacrylate
HEMA-PC	2-(Methacryloxyethyl)-2'-(trimethylammoniumethyl)phosphate
HS	Atom transfer agent compound
$[I_2]$	Concentration of initiator
Init	Initiator
k_β	Rate constant for β-scission
k_{add}	Rate constant of addition
k_{ct}	Rate constant for initiation of monomer through transfer
k_d	Rate constant of disassociation
k_i	Rate constant of initiation
k_p	Rate constant of propagation
k_t	Rate constant of termination
k_{tc}	Rate constant of termination by combination
k_{td}	Rate constant of termination by disproportionation
k_{tr}	Rate constant for initiation of monomer through transfer
L	Lens thickness
Lig	Ligand
LMA	Lauryl methacrylate
[M]	Concentration of monomer
[M•]	Concentration of primary radicals
MAA	Methacrylic acid

MeOPEGMA	Polyethylene glycol methyl ether methacrylate
M_i	Molecular weight of species *i*
MMA	Methyl methacrylate
Mn	Number average molecular weight
MPC	2-(Methacryloxyethyl)-2'-(trimethylammoniumethyl)phosphate
Mw	Weight average molecular weight
MWD	Molecular weight distribution
N_i	Number of moles of species *i*
NMR	Nuclear magnetic resonance
NORBLOC	2-(2'hydroxy-5'methacryloxyethyl-phenyl)-2*H*-benzotriazole
NOXCoBF	[Bis{μ-[1,2-cyclohexanedione dioximato(2-)O:O']}tetrafluorodiborato(2-)-*N*,*N*',*N*'',*N*''']cobalt
NVP	*N*-Vinylpyrrolidone
P*	Active polymer species
PDI	Polydispersity index
PDMS	Polydimethylsiloxane
PEG	Polyethylene glycol
PEGMA	Polyethylene glycol methacrylate
PP	Polypropylene mould
PPG	Polypropylene glycol
PMMA	Polymethyl methacrylate
PVC	Polyvinyl chloride
P-X	Polymeric alkyl halide initiator
r_a & r_b	Monomer reactivity ratios
RAFT	Reversible addition-fragmentation chain transfer
R_i	Rate of initiation
R_p	Rate of propagation
R_t	Rate of termination
R-X	Alkyl halide initiator
[S]	Concentration of chain transfer agent
SEC	Size exclusion chromatography
SEE	Silyl Enol Ether
SiGMA	Tris(trimethylsiloxy)silylpropylglycerol methacrylate

SPE	*N*,*N*-Dimethyl-*N*-methacryloxyethyl-*N*-(3-sulphopropyl)-ammonium-betain
TEMPO	2,2,6,6-Tetramethylpiperidinyloxy
TGA	Thermal gravimetric analysis
THF	Tetrahydrofuran
TM	Transition metal
TMM-LRP	Transition metal mediated living radical polymerisation
TMS	Trimethyl silyl
TRIS	Tris(trimethylsiloxy)-3-methacryloxy propylsilane
TSMC	Tris(trimethylsiloxy)silylpropylmethacryloxyethylcarbamate
UV	Ultra violet
UVAM	2-(2'Hydroxy-3-*t*-butyl-5-vinyl phenyl)-5-chloro-2*H*-benzotriazole
V601	2,2'-Azobisisobutyrate
w	Total weight of polymer
w_i	Weight of species i

Chapter 1

Introduction

1 Introduction

The area of polymer chemistry is extensive with many different types of polymers and methods by which they are synthesised. Historically two methods of polymerisation can be used to classify polymer types. Condensation polymers are defined as polymers produced via methods that produce small molecules, such as HCl or H_2O as well as high molecular weight polymer *e.g.* polyesters, *figure 1.0*.

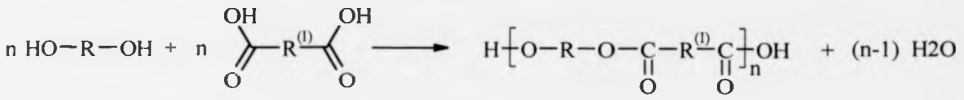


Figure 1.0, Synthesis of polyesters from a diol and a dicarboxylic acid

Addition polymers are polymers that have the same atoms in the repeat unit as in the monomer. This includes the polymerisation of all substituted ethenes such as vinyl chloride, styrene and methyl methacrylate, *figure 1.1*.

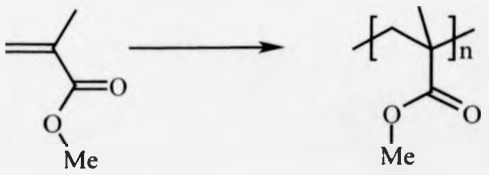


Figure 1.1, Formation of an addition polymer,
in this example polymethyl methacrylate

This method of classification can be ambiguous because a greater number of methods of polymerisation have arisen allowing the formation of certain polymers by more than one method. For example, polyethylene glycol, $\text{-}[\text{-}OCH_2CH_2\text{-}]_n\text{-}$, can be formed through condensation polymerisation of ethylene glycol or through the ring

opening polymerisation of ethylene oxide. This ambiguity has lead to the introduction of the two broader classifications of step growth and chain growth polymerisation. Step growth polymerisations occur by stepwise addition of reactants whereby all polymer molecules grow at a steady rate throughout the system. Primarily short chains form which then react with one another or additional monomers to eventually form long chain polymers. Examples of step growth polymerisations include condensation polymerisations such as the synthesis of polyesters and polyurethanes. Chain growth polymerisations can be further subdivided into conventional and living chain growth polymerisation. Chain growth polymerisations involve an initiation step to start the reaction followed by a propagation step. Typically initiating species include free radicals, anions, cations and complex co-ordination compounds which provide an active site for monomer to add via a chain reaction (propagation) until either all monomer is consumed or a termination or chain transfer step occurs. The result can be the production of a high molecular weight polymer almost instantaneously from when the active species is formed and thus polymer is produced continuously throughout the reaction. Living chain growth polymerisations differ from conventional chain growth in that no permanent chain-stopping reactions occur. This has the effect that molecular weight increases linearly with conversion. The differences are clearly seen if number average molecular weight is plotted against conversion as in *figure 1.2*.

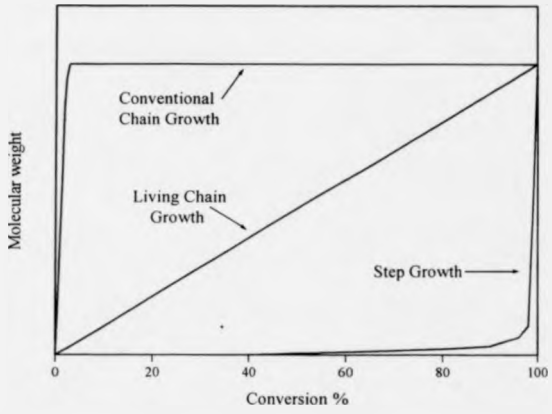


Figure 1.2, Molecular weight vs. conversion for step and chain growth polymerisations

The main part of this thesis concerns the two relatively new chain growth polymerisation techniques of catalytic chain transfer polymerisation (conventional chain growth) and transition metal mediated living radical polymerisation (living chain growth). In particular their application to the production of functional methacrylate polymers of interest to biomedical applications is examined.

1.1 Mechanism of Free Radical Polymerisation

Free radical polymerisation is industrially relevant due, in part, to the tolerance of trace impurities and versatility towards different reaction conditions. There is often no need for the rigorous purification of solvents, initiator or removal of stabilisers found in commercially available monomers. The presence of trace levels of oxygen or water often has no detrimental effect to the product. The robust nature of free radical polymerisations means that they may be carried out in water as the reaction medium, as in the case of suspension and emulsion polymerisations. These benefits have led to

free radical polymerisation being one of the most popular techniques used by industry.

Free radical polymerisation may be broken down into four processes; initiation, propagation, termination and chain transfer. Initiation, propagation and termination are outlined below for methyl methacrylate (MMA) however, chain transfer is discussed in *section 1.4.2.*

1.1.1 Initiation

A large number of free radical initiators are commercially available. For example, peroxides, such as dibenzoyl peroxide (BPO), azo compounds, such as 2,2'-azo-bis-isobutyronitrile (AIBN) and redox systems such as hydrogen peroxide / iron$^{(II)}$. Both peroxides and azo initiators undergo homolytic cleavage upon either heating or exposure to UV light to produce primary radicals, *figure 1.3.*

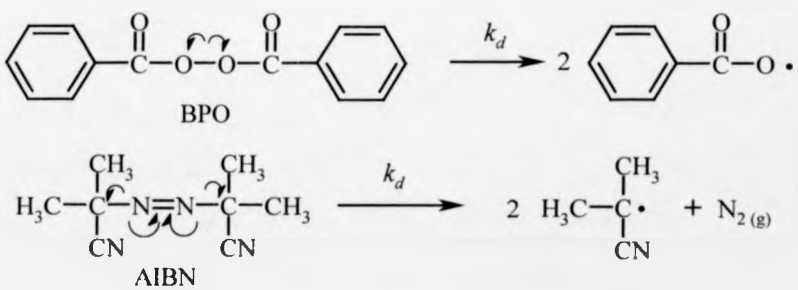


Figure 1.3, Formation of primary radicals from BPO and AIBN

The choice of initiator for a particular reaction is dependent upon several factors such as, reaction temperature, half-life, solubility in the reaction medium, reactivity

towards species other than monomer and sometimes required end group functionality; which may be dependent on the structure of either the initiator and/or the radical formed. Once formed radicals react with the carbon-carbon double bond of the monomer present to form initiating radicals, this is demonstrated for the reaction of the cyanoisopropyl radical (from AIBN) with MMA, *figure 1.4*.

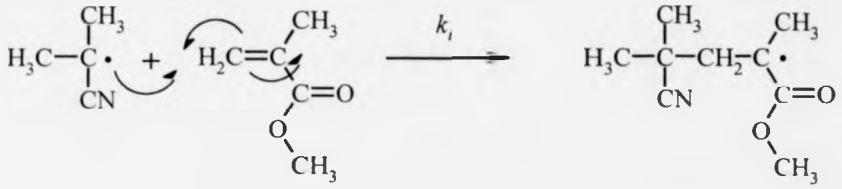


Figure 1.4, Reaction of primary cyanoisopropyl radical with MMA to form initiating radicals

It is noted that only tail addition is shown and the radical addition can be complicated by other possible reactions such as head addition. A large number of side reactions can also occur such as, reaction with oxygen, additives or any impurities present in the solvent or monomer, formation of initiator-derived by-products, fragmentation and rearrangement of radicals in addition to radical-radical terminations. These processes are not confined to the initiation step and can occur at any time during the polymerisation.

The overall rate of initiation (R_i) for the thermal decomposition of an initiator (for $I_2 \rightarrow 2I\bullet$) is given by the following rate expression:

$$R_i = 2 f k_d [I_2] \qquad \textbf{(1)}$$

where f = efficiency factor, k_d = rate constant of dissociation, $[I_2]$ = concentration of initiator.

It is assumed that the rate of dissociation of initiator is slower than the rate of primary radical addition to monomer such that $k_d << k_i$ (this only holds if monomer addition is fast). Due to the possible side reactions not all the primary radicals will go on to initiate polymer and therefore the efficiency factor f is introduced, f is defined as the ratio of the rate of initiation of monomer to the rate of initiator disappearance and is largely affected by solubility of the primary radical in the reaction medium. Typically f is in the range 0.3-0.8 but does not remain constant because as monomer is consumed the viscosity of the reaction medium increases.

1.1.2 Propagation

The second step of the polymerisation is the addition of monomer to the active end in a series of identical reactions, *figure 1.5*.

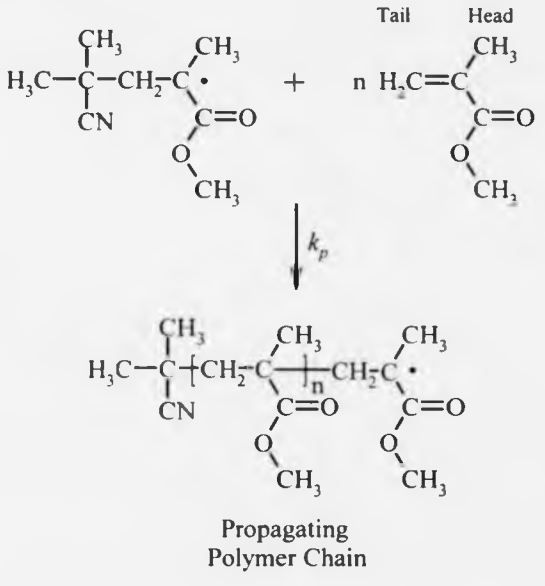


Figure 1.5, Propagation Step: reaction of initiating radical with monomer for MMA/PMMA

Head-to-tail addition is shown as this is the thermodynamically preferred product. Stereospecificity is an important consideration as head-to-head linkages can be responsible for producing weak links in a polymer structure which may lead to a decrease in the materials mechanical properties. This is rationalised by assuming that the propagation step is under thermodynamic control, *i.e.* that the formation of secondary or tertiary radicals is more stable than the formation of primary radicals occurring from head-to-head linkages. However, this is not always the case and it has been shown that radical reactions are equally as likely to be under kinetic control. This means that steric and polar influences can have a great effect on the proportion of head-to-tail linkages. Whilst these considerations affect the stereospecificity of addition they also influence the rate of addition. This is a complicated area and it is not the aim to give a full account of all the considerations here but a brief discussion

outlining the key points follows. Substituents on a double bond retard addition to the substituted carbon whilst addition to the non-substituted end will remain relatively unaffected. Therefore, there are few exceptions where radicals do not add preferentially to the less substituted end of olefins, to give head-to-tail addition. The rate of addition is thought to be primarily determined by polar factors. As one would expect electron-withdrawing substituents *e.g.* Cl, F, CO_2R, CN, enhance reactivity towards nucleophilic radicals and reduce reactivity towards electrophilic radicals. The inverse being true for electron-donating substituents *e.g.* alkyls. This will affect the rates of head-to-tail and head-to-head additions however generally an increase in rate of head addition is accompanied by an even greater rate of tail addition, the inverse being true when a reduction in rate is observed. Polar effects become more important in copolymerisations where the polarity of the comonomers differ and steric factors play a less important role due to their relatively small size. An example of this is the polymerisation of vinylidene fluoride where electrophilic radicals add via tail addition and nucleophilic radicals add via head addition. The relative polarities may also affect the relative reactivity of one monomer with another; this is discussed in more detail in *section 1.1.5.*

Propagation is best considered under steady state conditions, which leads to the following relationship, *equation 2*:

$$R_p = k_p [M][M^{\cdot}] \qquad (2)$$

There are a number of points to be considered . It is assumed that each reaction in the propagation sequence is identical and independent of chain length such that k_p remains constant. This is not the case for very short chain lengths. This model is only valid at low conversions when viscosity effects are negligible throughout the reaction. It is also assumed that the radical concentration remains constant and that

monomer consumption is equal to the rate of polymer formation. Propagation has no effect on the concentration of radicals as it merely transforms one radical species to another.

1.1.3 Termination

Termination by reaction of two long chain polymer radicals can occur by either combination or disproportionation.

a) Termination by Combination

Combination is the reaction of two polymer radicals in a head-to-head linkage, *figure 1.6*.

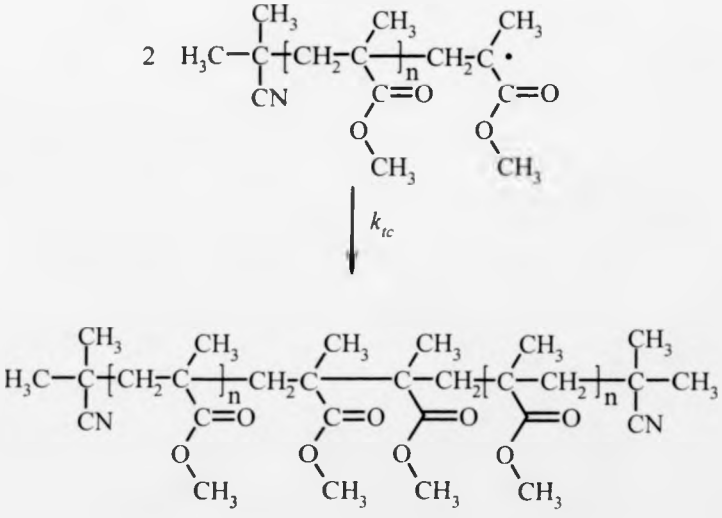


Figure 1.6, Mechanism of termination by combination for PMMA

The effect of this head-to-head linkage becomes more significant as the size of the substituent increases. Increasing the bulkiness of the substituent will cause a strained conformation that may produce a weak link in the polymer leading to a reduction in thermal stability.

b) Termination by Disproportionation

Disproportionation occurs via hydrogen abstraction by one propagating radical from another, *figure 1.7*. The result is two different types of terminal group, saturated and unsaturated.

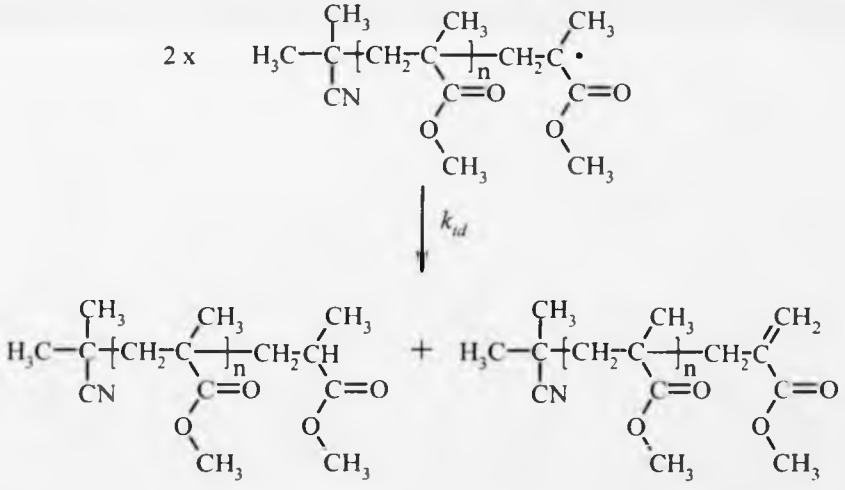


Figure 1.7, Mechanism of termination by disproportionation for PMMA

These two reactions occur simultaneously with the ratio k_{td}/k_{tc} being affected by a number of conditions. Termination in polymerisations of mono substituted olefins, acrylates and styrenics, occurs predominantly via combination[1]. Whereas in polymerisations of monomers containing an α-methyl substituent, methacrylates, the

product will show a high level of termination by disproportionation[1]. The level of combination tends to increase as the ability of the substituent to stabilise the radical increases. Temperature also has a marked effect on the relative ratios of combination to disproportionation as the latter requires a bond-breaking step and therefore has a greater activation energy than combination. Therefore if temperature is increased the difference in activation energy becomes less important and disproportionation becomes more competitive.

Termination is independent of the mechanism by which it occurs such that:

$$k_t = k_{tc} + k_{td} \qquad \textbf{(3)}$$

Therefore the overall rate of termination can be given by the following expression, given that termination involves a bimolecular reaction between two radicals, *equation 4*:

$$R_t = 2k_t[\mathrm{M}\bullet]^2 \qquad \textbf{(4)}$$

1.1.4 Trommsdorff Effect

In bulk or concentrated solution polymerisations a sudden increase in rate is often observed when the medium viscosity gets very high, this is known as the Trommsdorff or gel effect. As viscosity increases chain mobility is decreases, reducing the probability of the active chain end being in a position where termination can occur . Therefore a decrease in k_t and an increase in [M•] are observed. However, small molecules such as monomer are still able to diffuse to the reactive chain end causing an increase in the rate of polymerisation. As addition polymerisation is exothermic the heat generated, which cannot dissipate, leads to a further increase in

rate. Under these nonisothermal conditions the process is known as an auto-acceleration and is usually undesirable.

1.1.5 Copolymerisation

Copolymers are important in many applications as they offer the opportunity to extend the physical properties available for two or more monomers. There are four different types of copolymers, these are random, alternating, block and graft. Random, or statistical, copolymers are formed when two or more monomers with similar reactivity are present in a system. Alternating copolymers consist of a series of comonomer units which alternate constantly throughout the polymer chain which occurs for a few specific monomer pairs. Block copolymers are composed of two or more blocks of different materials. Graft copolymers are composed of a polymer chain of one monomer with polymers attached along the backbone. Block and graft copolymers are formed by a variety of routes, some of which will be discussed in this thesis. The four types of copolymer are summarised in *figure 1.8*, whereby A and B represent the two different monomers from which the polymers are formed.

AABABABBBBABBAAAB Random copolymer

ABABABABABABABA Alternating copolymer

AAAAAAAAABBBBBBBB Block copolymer

AAAAAAAAAAAAAAAA Graft copolymer
B B B
B B B
B B B
B B B
B B B
B B B
B B B

Figure 1.8, Types of copolymer available

1.1.5.1 Statistical Copolymerisation

In order to fully describe a copolymerisation a large number of parameters need to be described. If the relative reactivity of two different monomer derived radicals differ then the composition of the reaction medium changes throughout the course of a reaction. Several models have been proposed to help explain copolymerisation. The two most common being the terminal model and the penultimate model.

a) Terminal Model

It is assumed that all chain ends A• are equally as reactive regardless of chain length or the penultimate unit, the same is true for chain ends B•. It is also assumed that the concentration of propagating chains remains constant as in a homopolymerisation. Applying these assumptions for the copolymerisation between two monomers, A and B, there are four possible reactions during propagation, *figure 1.9*.

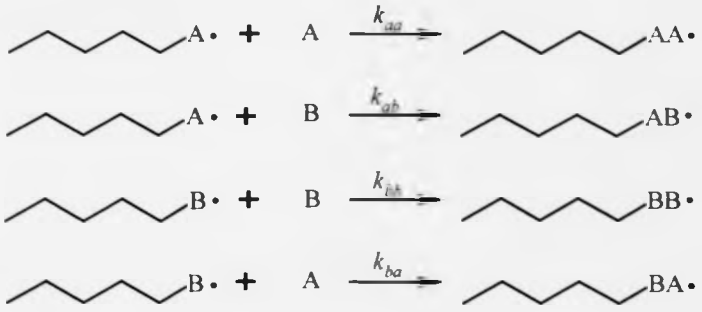


Figure 1.9, Terminal model for copolymerisation kinetics in free radical polymeiration

The rate constants of these reactions are all different and vary according to monomer functionality, solvent system and temperature and are obviously dependent upon concentration. Therefore it follows that consumption of the two monomers occurs at different rates. This leads to a change in concentration throughout the reaction and thus a continuous change in rate. This leads to an associated compositional drift throughout the polymer. Through examination of these rates and consideration of the assumptions the copolymer equation **(5)** can be derived.

$$\frac{\delta[A]}{\delta[B]} = \frac{[A]}{[B]} \frac{r_a[A]+[B]}{r_b[B]+[A]} \qquad \textbf{(5)}$$

Where r_a and r_b are the reactivity ratios for the growing chain with monomer of its own type with respect to the other monomer; *i.e.* r_a is the ratio of the reactivity of the propagating chain $A^{\bullet}$ with monomer A compared to reactivity with monomer B, as defined in *equation 6*.

$$r_a \equiv \frac{k_{aa}}{k_{ab}} \qquad r_b \equiv \frac{k_{bb}}{k_{ba}} \qquad (6)$$

The reactivity ratios give information about the compositional drift throughout the reaction. In order to measure these ratios it is convenient to describe the copolymer composition and feed ratios in terms of mole fractions. If F_A is the mole fraction of A in the polymer and f_a the mole fraction of A in the feed then it follows:

$$F_A = 1 - F_B = \frac{\delta[\mathrm{A}]}{\delta[\mathrm{A}] + \delta[\mathrm{B}]} \quad \text{and} \quad f_a = 1 - f_b = \frac{[\mathrm{A}]}{[\mathrm{A}] + [\mathrm{B}]} \qquad (7)$$

Substitution of equations **5. 6** and **7** gives us an equation **8** relating copolymer composition to the feed composition and the reactivity ratios:

$$F_A = \frac{r_a f_a^2 + f_a f_b}{r_a f_a^2 + 2 f_a f_b + r_b f_b^2} \qquad (8)$$

Five cases are defined:

- $r_1 = r_2 = 0$ In this case A˙ reacts with B and B˙ with A. The result is an alternating copolymer.
- $r_1 = r_2 = 1$ There is no preference and the copolymerisation is completely random.
- $r_1 >> 1$ and $r_2 << 1$ meaning that the copolymer remains very rich in polymer A until the concentration diminishes. Resultant polymer has a composition similar to that of a block copolymer.
- $r_1.r_2 = 1$ The propagating chains have the same preference for either monomer independent of the terminal unit. This is defined as ideal copolymerisation when both r_1 and r_2 are close to 1, however the more they diverge the less random the distribution will be.

- r_1 & r_2 are both between 0 and 1. This is typical of a statistical copolymerisation somewhere between an alternating and a random copolymer and is known as an azeotropic polymerisation.

b) Penultimate Model

In the majority of cases the terminal model adequately describes both the instantaneous copolymer composition and sequence distributions[2]. However, the model fails to accurately define the overall rate of propagation which often shows deviations from the predictions of the terminal model using monomer reactivity ratios obtained from composition data[2]. Merz *et al.* were the first to propose that the penultimate unit had an effect on the reactivity of the radical centre and so formulated the penultimate model[3]. Fukuda *et al.* used this formula to explain the observed deviations in k_p from those predicted by the terminal model for a number of copolymerisations of MMA / Styrene[4,5]. The model, one of the simplest in its formulation, accurately describes both the copolymer composition and the overall rate of propagation. This model has eight different propagation steps leading to six different reactivity ratios. As with the terminal model the instantaneous copolymer composition is determined by the monomer reactivity ratios. The main difference to the terminal model lies in the introduction of the radical reactivity ratios into the expression for the overall propagation rate coefficient. The theoretical justification of the penultimate unit effect is the subject of many articles[6,7]. The first rationalisation was the stabilisation energy model proposed by Fukuda *et al.* This model is based on the penultimate unit affecting the stability of the propagating radical, *i.e.* solely on enthalpic effects[8]. Through evaluation of copolymerisation data the validity of this

model was shown to be limited[9,10]. A more general version of the model has since been proposed by Fukuda *et al.* providing a significantly improved model[11]. Whilst not disputing that the penultimate unit will affect the activation energy, it was proposed by Bamford and Basahel that steric effects will contribute to radical reactivity[12,13]. Subsequent studies by Heuts *et al.* indicate that penultimate effects could indeed be explained, in part, by variations in the entropy of activation[6,14].

1.2 Polymerisation Processes

Free radical polymerisation can be carried out in four main polymerisation systems: bulk, solution, suspension and emulsion, each with associated benefits and drawbacks. The system used is mainly dependent upon the nature of the product required however the polymerisation method may well be a consideration.

1.2.1 Bulk Polymerisation

Polymerisations are carried out in absence of solvent. The benefits include reduced material cost and processing expenditure as there is no need for removal of residual solvent, assuming complete monomer consumption. The polymer is ready for direct processing or polymerisation can be carried out in specific moulds. Bulk polymerisations, however, are very difficult to control due to the Trommsdorf effect and problems associated with reduced heat transfer at high conversion. Examples of bulk polymerisation include the formation of Perspex© (PMMA).

1.2.2 Solution Polymerisation

Solution polymerisation is similar to bulk polymerisation with the addition of an appropriate solvent. Due to the gel or Trommsdorf effect it is often necessary for the addition of solvent to facilitate heat transfer which is achieved by the lowering of viscosity that the solvent imparts. Choice of solvent is particularly important because reactions to the solvent such as chain transfer must be avoided. Poisoning of catalyst by solvent impurities must also be considered and can lead to increased production costs if there is a need for purification. Solution polymerisation is useful when polymers are to be applied in solvent as in the case of coatings, casting of films and solution spinning of fibres. The polymerisation of styrene is a useful example where styrene itself is used as the solvent and conversions are only taken to 30 % with the monomer being recycled.

1.2.3 Suspension Polymerisation

Monomer and initiator are placed in a non-solvent, typically water, and through vigorous stirring and the presence of soluble suspension agents monomer particles are formed, 0.1 – 1 mm in diameter. Polymerisation occurs in these particles analogous to the bulk polymerisation. If suspension agents are not deployed and agitation not maintained coagulation of polymer particles may occur. Heat removal is easy thus auto-acceleration is not a consideration and as such this is a very useful method for polymerisations that are very exothermic, as in the case of styrene and vinyl chloride. Polymer produced by suspension polymerisation is in the form of granules that are ready for processing.

1.2.4 Emulsion Polymerisation

Emulsion polymerisation, like suspension polymerisation, is a heterogeneous process. The notable differences are in the mechanism of the polymerisation. No suspension agent is used although surfactants are often required to help stabilise monomer droplets and form micelles in which the polymerisation occurs. Initiation occurs in the water phase where little monomer is present. As the chains grow they migrate into the micelles formed by the surfactant. Monomer migrates from the droplets through the water phase feeding the propagating chains. It is important to continue agitation throughout the polymerisation in order to maintain the emulsion. Once the reaction is complete and the monomer droplets have been consumed the emulsion is stable. Products are often used directly as formed as in the case of water-soluble paints and adhesives. Heat transfer and viscosity are unproblematic and as emulsions are carried out in water the method is considered to be more environmentally friendly. Due to the unusual chain of events in emulsion polymerisation the kinetics and mechanism are considerably different to that of other types of polymerisations.

1.3 Molecular Weight of Polymers

Polymers are formed by successive random encounters of reactive species and therefore it is unsurprising that they are not discrete molecules, instead they are a mixture of molecules with different molecular weights. Therefore polymer molecular weight is concerned with the statistical description of averages. The most commonly used are the number average molecular weight, Mn, and the weight average molecular weight, Mw. Degree of polymerisation, DP, is another way of expressing the size of a

polymer, it describes the average number of monomer units in the polymer. The number average degree of polymerisation (DP_n) and the weight average degree of polymerisation (DP_w) being calculated through division of *Mn* or *Mw*, respectively, by the formula weight of the monomer.

1.3.1 Number Average Molecular Weight

The total weight, *w*, of a polymer sample can be expressed by the following equation **(9)**:

$$w = \sum_{i=1}^{\infty} w_i = \sum_{i=1}^{\infty} N_i M_i \qquad \textbf{(9)}$$

Where w_i, N_i and M_i are the weight, number of moles and the molecular weight of each species, *i*, respectively.

The number average molecular weight is determined from an analysis of the total number of polymer molecules in a polymer sample, *i.e.* it is the total weight of the polymer sample divided by the number of molecules in that sample. Therefore it follows that *Mn* can be described by the following equation **(10)**:

$$Mn = \frac{w}{\sum_{i=1}^{\infty} N_i} = \frac{\sum_{i=1}^{\infty} N_i M_i}{\sum_{i=1}^{\infty} N_i} \qquad \textbf{(10)}$$

Determination of *Mn* relies on analysis methods that count the number of polymer molecules in a sample. Such methods examine the concentration of molecules present in a solution. Examples include titration of end groups, vapour pressure osmometry and membrane osmometry.

1.3.2 Weight Average Molecular Weight

The weight average molecular weight is dependent on the weight fraction of each molecular species rather than the quantity of each molecular species as in the case of *Mn*. This means that the larger the molecule the greater its contribution to the value of *Mw*, as such *Mw* is always larger than *Mn*. *Mw* is defined as follows, *equation 10*:

$$Mw = \frac{\sum_{i=1}^{\infty} w_i M_i}{\sum_{i=1}^{\infty} w_i} = \frac{\sum_{i=1}^{\infty} N_i M_i^2}{\sum_{i=1}^{\infty} N_i M_i} \qquad \textbf{(11)}$$

Mw determination relies upon methods analysing the mass of the species present. Such methods include light scattering and ultracentrifugation.

1.3.3 Polydispersity Index

Polymers are a mixture of macromolecules with different molecular weights and as such they have a mass distribution. The ratio between *Mn* and *Mw* is expressed as the polydispersity index, PDI, which provides information concerning the distribution of chain lengths for the polymer sample. For a monodisperse sample the PDI would be equal to 1, polymerisation techniques exist which allow control over the PDI and values approaching 1 have been reported. However, due to the statistical nature of free radical polymerisations a wide distribution in molecular weights is observed and values around 2 are more common. The PDI of polymers is an important characteristic as it can significantly affect polymer properties.

1.3.4 Kinetic Chain Length

An alternative way of expressing the length of a polymer chain is the kinetic chain length, ν. This is related to the concentration of initiator and is defined as the average number of monomer molecules consumed per primary radical. Assuming steady state ν is equal to the ratio of R_p to R_i and given that R_i is equal to R_t it can also be expressed as the ratio of R_p to R_t to give *equation 12*:

$$\nu = \frac{R_p}{R_i} = \frac{R_p}{R_t} \qquad \textbf{(12)}$$

Substitution of the termination and overall polymerisation rates and in turn the steady state expression for radical concentration allows an equation to be derived which shows that the kinetic chain length is inversely proportional to the square root of the initiator concentration, *equation 13*:

$$\nu = k[\mathrm{I}]^{-\frac{1}{2}}[\mathrm{M}] \qquad \textbf{(13)}$$

Thus any increase in initiator concentration will result in a decrease in the kinetic chain length and therefore the molecular weight of the polymer.

1.4 Molecular Weight Control in Free Radical Polymerisation

The physical properties of polymers are heavily dependent upon chemical structure and degree of branching and also upon molecular weight. Mechanical strength, viscosity and melt flow, and thus processability, are all dependent upon molecular weight. As these physical properties are dependent on molecular weight then the

polydispersity is also an important property with respect to mechanical properties. Free radical polymerisations are typically thought of as unselective affording little control over both molecular weight and polydispersity index. In free radical polymerisation there are two traditional methods of controlling these properties, these are an increase in initiator concentration or the use of a chain transfer agent. In more recent years polymerisation techniques have been developed that allow greater control over these properties, these include catalytic chain transfer polymerisation and transition metal mediated living radical polymerisation (*sections 1.5 & 1.6.3* respectively).

1.4.1 Initiator Concentration as Control of Molecular Weight

The correlation between the kinetic chain length and initiator concentration has been discussed in *section 1.3.4*. To achieve very low molecular weights it is often necessary to use very high concentrations of initiator, which is impractical owing to the high cost of initiators and also toxicity considerations. Furthermore, high concentrations of initiator will result in high levels of termination by primary radicals. Using initiator to control molecular weight is therefore very limited. Increasing dissociation of the initiator (*i.e.* increase of temperature) will have the same effect in reduction of molecular weight, however it will also have the same associated drawbacks.

1.4.2 Chain Transfer

Chain transfer is the termination of a propagating polymer chain by the transfer of the radical to produce a new radical species which subsequently initiates a new chain. There are at least two basic mechanisms for chain transfer; these are atom or group transfer and addition-fragmentation. Chain transfer can occur to monomer, solvent, initiator or deliberately added small molecules called chain transfer agents (CTA). The net effect of chain transfer is to reduce the chain length by increasing the number of chains. Therefore chain transfer agents are often added to polymerisation systems to control molecular weight.

a) Atom or Group Transfer

Atom or group transfer, as the name suggests, involves transfer of a hydrogen atom or other small moiety from the chain transfer agent to the propagating chain via a homolytic substitution mechanism. This yields a dead polymer chain and a new radical which can proceed to initiate a new propagating chain. This is demonstrated in *figure 1.10* for the transfer of a hydrogen atom from a molecule (HS) in the polymerisation of MMA.

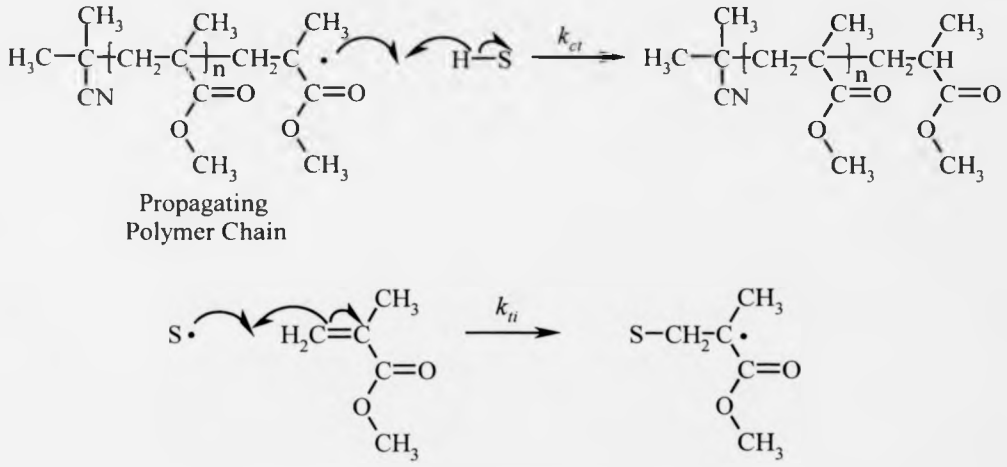


Figure 1.10, Chain transfer in free radical polymerisation of MMA

k_{ct} is the rate constant for chain transfer and k_{ti} the rate constant for the initiation of monomer through the radical species formed from the transfer. Rate constants are determined by a combination of bond strengths, steric and polar factors. If $k_{ti} = 0$ and $k_{ct} >> k_p$ then the transfer compound is an inhibitor. Such compounds are termed 'radical scavengers' and are used to prevent premature polymerisation. The extent of chain transfer and the effect on the rate of polymerisation are dependent upon the relative rate constants of propagation and chain transfer. If $k_{ti} \geq k_p >> k_{ct}$ then normal chain transfer occurs but whilst there is a decrease in molecular weight the rate of polymerisation is unaffected. Where $k_{ti} < k_p$ the rate in polymerisation is retarded and if $k_p << k_{ct}$ the effect is so great as to cause a very large decrease in both the rate of polymerisation and molecular weight.

Typical examples of chain transfer agents are carbon tetrahalides, mercaptans and tertiary amines. It is important to note that these compounds become incorporated into the polymer, which provides a method of controlling end group functionality.

However, this methodology of chain transfer means that high concentrations of CTA are required if products of very low molecular weights are desired. This can be problematic due to the toxicity, odour and colouration associated with these types of compounds.

b) Addition-Fragmentation

An alternative mechanism by which some transfer agents react is that of addition-fragmentation. This is a three-step process whereby a short-lived intermediate is formed. Typically this occurs with certain unsaturated compounds having the general structure outlined in *figure 1.11*, where R is a group chosen to give the transfer agent an appropriate reactivity with respect to the monomer and Y or Z is a radical leaving group.

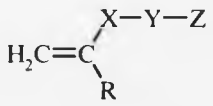


Figure 1.11, General structure of an unsaturated addition-elimination chain transfer agent

The mechanism of addition-fragmentation is summarised in *figure 1.12* for the reaction between a propagating PMMA chain with a vinyl ether. The radical formed on reaction of the propagating chain with the vinyl ether is stericly hindered and therefore β-scission occurs. β-scission is an intramolecular rearrangement fragmenting the molecule to yield terminated polymer and a new radical.

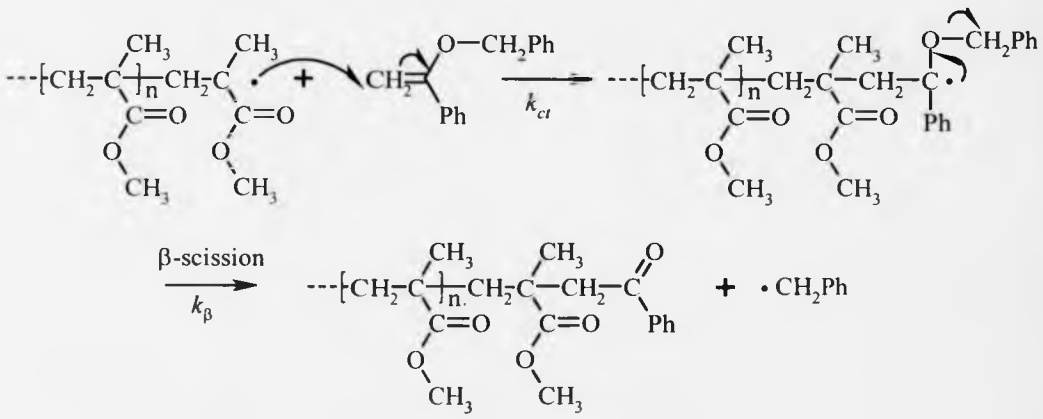


Figure 1.12, Addition-fragmentation mechanism exemplified for reaction between a PMMA propagating chain and a vinyl ether.

Reactivity of these types of chain transfer agents is determined by both their reactivity towards the propagating species and the properties of the intermediate formed. If the intermediates lifetime is significant (k_β slow) then reactions other than β-scission may occur. If coupling or disproportionation with another radical occur the polymerisation will be retarded, and if monomer addition occurs the compound is an inefficient transfer agent.

1.4.2.1 Determination of Chain Transfer Constants

The effectiveness of a chain transfer agent is dependent upon the ratio of k_p and k_{ct} which are dependent upon a combination of bond strengths, steric and polar factors. Therefore the efficiency of a chain transfer agent is affected by monomer composition, reaction medium, initiator concentration and temperature. It follows that the degree of polymerisation will be dependent upon the ratio of the concentrations of

chain transfer agent to monomer. Through kinetic analysis the following equation **(14)** can be derived:

$$\frac{1}{DP_n} = \frac{1}{DP_{n0}} + \frac{k_{ct}[S]}{k_p[M]} \qquad \textbf{(14)}$$

DP_{n0} represents the degree of polymerisation without chain transfer agent and [S] and [M] are the concentration of chain transfer agent and monomer respectively at time zero. The chain transfer constant, *Cs*, is a term introduced to express the ratio of k_{ct}/k_p. Following simple rearrangement and substitution we arrive at the *Mayo-equation* **(15)**[15]:

$$\frac{1}{DP_n} - \frac{1}{DP_{n0}} = \frac{Cs[S]}{[M]} \qquad \textbf{(15)}$$

A $Cs = 1$ is ideal as under this circumstance the transfer agent : monomer ratio will remain constant throughout the polymerisation, therefore DP_n remains constant. If $Cs >> 1$ then R• reacts faster with the chain transfer agent than with monomer causing a change in the ratio of transfer agent : monomer with conversion. This results in an increase in molecular weight with conversion and a broadening of the polydispersity index. The inverse is true if $Cs << 1$ then the transfer agent will be consumed slowly and the transfer agent : monomer ratio will increase causing a lowering in the molecular weight of polymer produced again leading to a broadening of the polydispersity index.

There are a number of ways in which the *Cs* for any given system can be calculated. The most common methods are based on the *Mayo-equation* and typically more than one value will be reported in each study. Experimental determination of a *Cs* value is carried out by a series of identical polymerisations with only a variation in the

concentration of chain transfer agent. The molecular weights of the resultant polymers are determined (typically by size exclusion chromatography, *section 7.1.1.2*) and the experimental $1/DP_n$ and $1/DP_{n0}$ values substituted into the *Mayo-equation* to give a *Cs* value for each chain transfer agent concentration. The *Cs* for the system is then quoted as an average of these *Cs* values. It should be noted that it is important to keep conversion to a minimum (typically less than 10 %) as the ratio of [chain transfer agent] : [monomer] will inevitably change (unless *Cs* = 1). Alternatively it can be seen from the *Mayo-equation* that a plot of [S]/[M] vs. $1/DP_n$, known as a *Mayo-plot,* will give a straight line with gradient equal to *Cs*.

A variation on these two methods uses the weight average degree of polymerisation (DP_w) instead of DP_n[16]. This method is beneficial to the standard *Mayo* methods when molecular weight information is obtained by size exclusion chromatography. This is due to the relative sensitivity of *Mn* values to baseline deviations compared to the relative insensitivity of *Mw* to such deviations[17,18]. In a chain transfer dominated system $DP_w/DP_n = 2$ therefore in the *Mayo-equation* the term DP_n is substituted with $DP_w/2$ to give *equation 16*:

$$\frac{2}{DP_w} - \frac{2}{DP_{w0}} = \frac{Cs[S]}{[M]} \qquad \textbf{(16)}$$

This form of the *Mayo-equation* can then be used to give two alternative *Cs* values, one through substitution of the experimentally determined DP_w values into the equation the other through a plot of [S]/[M] vs. $2/DP_w$.

More recently Clay and Gilbert derived an equation that shows equivalent information can be obtained through analysis of the slope of a molecular weight distribution (Λ),

when plotted as the natural logarithm of the number distribution (ln(P(M)) against molecular weight, *equation 17*[19]:

$$\lim_{M\to\infty}\frac{\mathrm{d}\ln \mathrm{P}(M)}{\mathrm{d}M} = \Lambda = -\left\{\frac{\langle k_t\rangle[\mathrm{R}\cdot]}{k_p[\mathrm{M}]} + Cm + Cs\frac{[\mathrm{S}]}{[\mathrm{M}]}\right\} m_0^{-1} \qquad \textbf{(17)}$$

where m_o is the mass of the monomer. A plot of $-\Lambda m_o$ vs. [S]/[M] gives a straight line with a slope equal to the chain transfer constant *Cs*. This procedure is known as the chain length dependent (CLD) method. One draw back with this method is that it requires the analyst to use his or her own discretion when selecting the area of the slope from which values are calculated. Although it is recognised that the slope should be taken at the higher end of the molecular weight distribution some reports claim more reliable results are obtained when Λ is determined in the region of the peak molecular weight[16,20,21].

Some examples of chain transfer agents and their chain transfer constants to MMA in bulk at 60 °C as determined through the *Mayo-equation* are shown in *table 1.1*.

Table 1.1, Chain transfer constants of various chain transfer agents in bulk polymerisation of MMA at 60 °C

Chain Transfer Agent	Chain Transfer Constant (*Cs*)
p-Anisoyl disulfide	14.6
Ph-SH	2.7
n-BuSH	0.67
Mercaptoacetic acid	0.63
Mercaptoethanol	0.62
CBr_4	0.27
CCl_4	2.4
Triethylamine	8.3

1.5 Catalytic Chain Transfer Polymerisation

Catalytic chain transfer polymerisation (CCTP) was developed from the recognition of a biological process dependent on Vitamin B_{12}, *figure 1.13*. The vitamin is constructed from a corrin ring with a cobalt atom in the centre covalently bonded to the 5' carbon of an adenosyl group. Vitamin B_{12} facilitates many enzymatic processes, most of which involve catalysis of a free radical intramolecular rearrangement. The process is dependent on division and formation of the Co-C bond. The biological process takes advantage of the perfect ratio between stability and lability of this weak σ-bond (20-30 $kJmol^{-1}$). It is the only homolytic cleavage reaction of its type in biochemistry, and all other cleavage reactions proceed via ionic species[22,23]. It was nature's use of this Co-C bond and the recognition that this novel chemistry may be applied to polymer science that led to the development of catalytic chain transfer polymerisation.

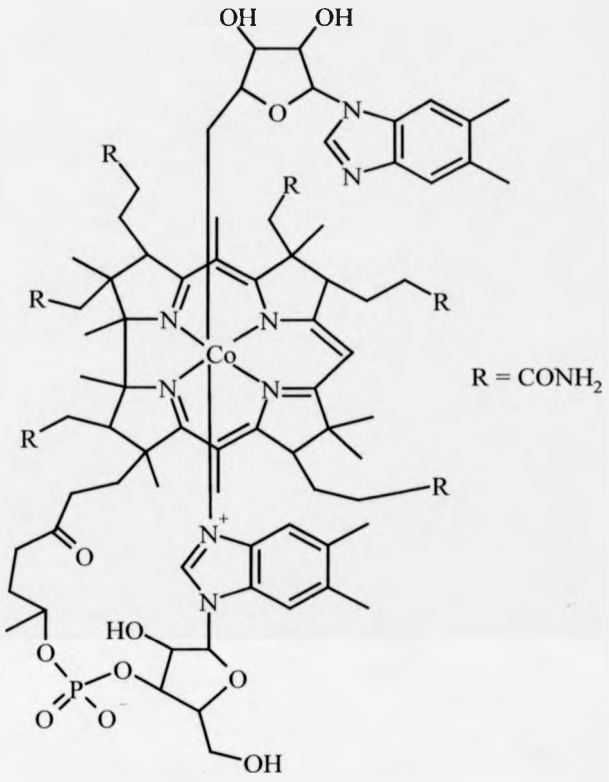


Figure 1.13, Structure of vitamin B_{12} coenzyme

Enikolopyan was the first to report the use of a vitamin B_{12} analogue as a chain transfer agent in 1975[24]. The analogue was a cobalt porphyrin that unlike the corrin ring of vitamin B_{12} is fully conjugated, *figure 1.14*.

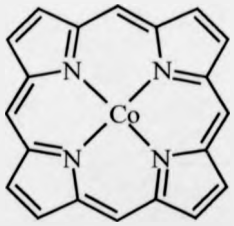


Figure 1.14, Structure of the cobalt porphyrin used by Enikolopyan

Enikolopyan demonstrated that cobalt porphyrins (Co-por) reduce the degree of polymerisation for methyl methacrylate from DP_n = 4100 to DP_n = 8.1 when the porphyrin was introduced at very low levels (6.1×10^{-4} M). This suggested a different mechanism for the chain transfer process, as the concentration of polymer was three orders of magnitude higher than that of the porphyrin. Through extraction of the porphyrin in a quantitative amount it was proven that there was no addition to polymer. It was concluded that there was CCT to monomer. Through the analysis of the Co-Por throughout the reaction it was determined that there was rapid interaction between the Co-Por and the polymer radical. NMR analysis of oligomeric products showed that they contained an unsaturated end group which has been confirmed through extensive NMR analysis[24], thermal gravimetric analysis[25] (TGA) and mass spectrometry[26]. It should be noted that this system only worked efficiently for monomers containing an α-methyl group, such as methacrylates.

In accordance with these findings and kinetic analysis Enikolopyan proposed two different mechanisms as the only feasible solutions. The first involves activation of the monomer by the porphyrin with subsequent chain transfer to this monomer **(18)**. The second mechanism is the abstraction of hydrogen from the propagating chain by the Co-por to form a cobalt hydride that is then able to initiate monomer **(19)**, see *figure 1.15*.

$$\text{MMA} + \text{Co-Por} \rightleftharpoons [\text{MMACo-Por}]$$
$$[\text{MMACo-Por}] + M_n^{\cdot} \longrightarrow M(=) + \text{Co-Por} + M_1^{\cdot} \quad \textbf{(18)}$$

$$M_n^{\cdot} + \text{Co-Por} \longrightarrow M_n(=) + \text{HCo-Por}$$
$$\text{HCo-Por} + \text{MMA} \longrightarrow M_1^{\cdot} + \text{Co-Por} \quad \textbf{(19)}$$

Figure 1.15, First proposed mechanisms for catalytic chain transfer polymerisation

In 1980 Smirnov *et al.* [27] presented evidence for the formation of the cobalt hydride through kinetic studies, later supported by the findings of O'Driscoll[28] and Gridnev[29]. Since the original studies, much work has been carried out in the area of catalytic chain transfer polymerisation with evidence growing to support the second of the mechanisms originally proposed by Enikolopyan[30,31].

The mechanism in its current form, whilst not accounting for all observed anomalies is now commonly accepted and can be represented by the following catalytic cycle for MMA, *figure 1.16*[32].

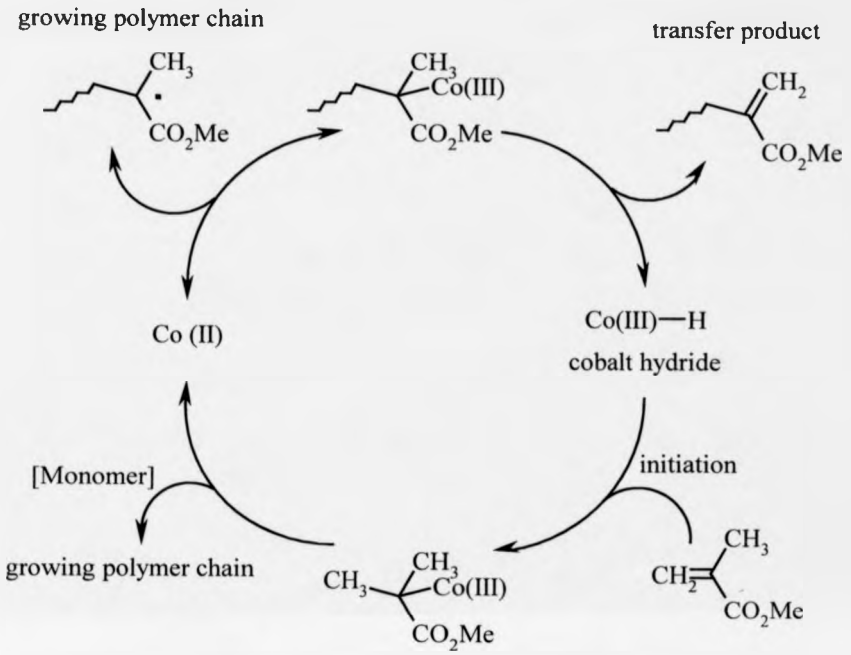


Figure 1.16, Generally accepted catalytic chain transfer mechanism

It can be seen that the Co(II) chain transfer agent does not become permanently attached to the polymer, as in the case of traditional chain transfer agents. Instead it is free to facilitate further chain transfer and it is this aspect of the polymerisation that is described as catalytic. The catalytic nature allows production of low molecular weight oligomers using only very small quantities of CCTA[30]. This eliminates many of the problems associated with the need for high concentrations of conventional chain transfer agents as discussed earlier *viz.* toxicity, odour and cost.

The cycle is deceptive in that it shows production of radicals to be catalytic as well however, this is not true as other reactions are taking place within the system, as shown by Davis *et al.* who observed that polymerisation will not proceed if initiator is depleted[32]. This suggests that reactions of Co(III) hydride to produce Co(II) exist

other than that of transfer to monomer, the most probable being reaction with small organic compounds.

For monomers containing an α-methyl group termination and initiation are principally by the chain transfer route therefore products contain an unsaturated end group and no initiator functionality.

1.5.1 Catalytic Chain Transfer Agents

As discussed the first catalytic chain transfer agent (CCTA) utilised was a porphyrin (hematoporphyrin IX tetramethyl ether) introduced by Enikolopyan, *figure 1.14*[24]. Many other porphyrins have been tested with varying degrees of success[33-35]. The porphyrins were found to have *Cs* in the range 1000-2400 for MMA, values some 3 orders of magnitude greater than mercaptans. Porphyrins with metal centres other than cobalt (Rh, Pd, Fe, Cu and Zn) were tested however no chain transfer activity was detected. Neither was there any activity when the simple porphyrin was tried (absence of metal centre). Whilst far better than standard CTAs the cobalt porphyrins were not suitable for industrial implementation[24]. This is due to their poor solubility in polar solvents, high oxygen sensitivity and strong colour due to the delocalised ring. By varying the axial ligands it was found that some of the problems could be over come, however at that time O'Driscoll was examining the effectiveness of a cobaloxime (R = Me) as a chain transfer agent[30]. Cobaloximes are commonly used for comparative purposes with porphyrins due to their easy synthesis from cobalt(II) acetate tetrahydrate and corresponding glyoxime, *figure 1.17*[36].

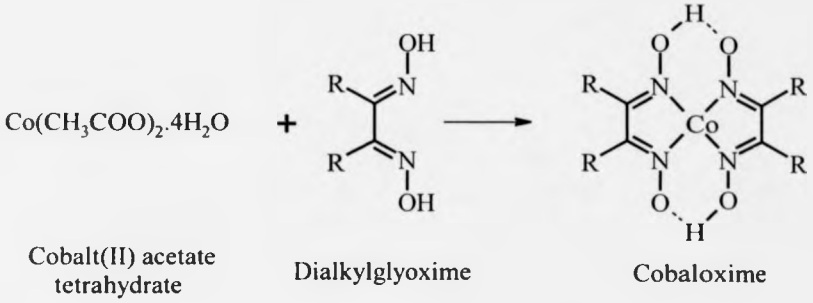
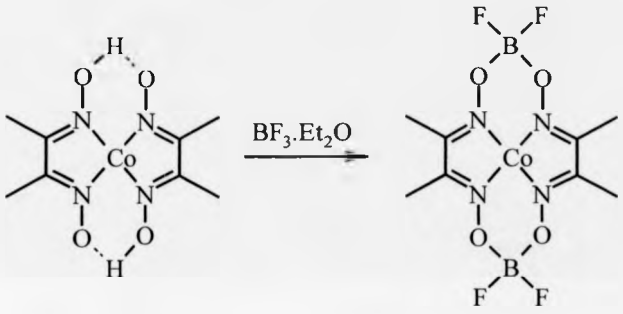


Figure 1.17, Synthetic route for the preparation of cobaloximes

Rempel *et al.* have shown that cobaloxime interacts with MMA by a process analogous to the mechanism proposed for CCTP[37]. Whilst more oxygen sensitive than the porphyrins the cobaloxime has better solubility, is cheaper and less coloured due to its semi-conjugated ring. It has also been shown that cobaloximes can be prepared by a simple method in situ prior to polymerisation[36]. Problems of oxygen sensitivity were overcome to some extent by co-ordination of a base ligand, triphenyl phosphine, in the axial position. O'Driscoll calculated the *Cs* values of various cobaloximes in the bulk polymerisation of MMA at 60 °C to be in the region 2×10^3 - 10^4 substantially higher than for the porphyrins. Gridnev followed up this work and examined a multitude of cobaloximes with various R substituents (CH_3, Ph, $COCH_3$ *etc.*) and axial ligands (Py, Cl, NO_2, CN *etc.*)[38]. It was found that changing these properties of the complex had a marked effect on activity. Co-ordination to cyano and nitro groups eliminated catalytic activity, whereas addition of bases increased activity (stronger bases cause stronger activity). In 1985 a variety of cobaloximes were patented for their use in CCTP by The Glidden Company[39].

Sanayei *et al.* reported that the effectiveness and stability of the cobaloxime could be improved by addition of BF_2 bridging moiety[28]. It was reported that cobaloxime boron fluoride (CoBF) had a *Cs* for MMA in bulk at 60 °C of $2.4\text{-}4.0\times10^4$. Synthesis of this complex had previously been reported by Bakac and Espenson and involves the simple reaction of cobaloxime with boron trifluoride etherate, *figure 1.18*[40].



Cobaloxime

Cobaloxime boron fluoride (CoBF)

Figure 1.18, Synthesis of CoBF from cobaloxime through incorporation of BF_2 bridging

Variation of the BF_2 bridging and the methyl groups of the glyoxime allows modification of the compounds stability and activity[41]. Many of these complexes have been patented by Janowicz for DuPont, one of the most important of which is CoBF. The importance of CoBF is due to its very high chain transfer activity and its relative stability, it is also stable in neutral aqueous media making it suitable for emulsion polymerisations[42-45].

In 1987 Gridnev *et al.* examined the properties of many active and inactive cobalt complexes from previous literature along with a series of tetraaza and diazodioxa complexes previously unexplored. This enabled them to put forward some simple

criteria to help in predicting the effectiveness of a compound as a CCTA as outlined below[34].

The electronic configuration of the cobalt is of primary importance. Cobalt (d7) can exist in high and low-spin states, three and one unpaired electrons respectively, and it has been found that only low-spin complexes are active CCT agents. The energy levels of the two spin states are close together meaning that the ligand plays an important role in deciding the spin state. Macrocycles should contain no less than three nitrogen donor atoms, although typically they contain four. The compound must contain at least a semi-conjugated system of π-bonds and carry one or two delocalised negative charges.

1.5.2 Factors Affecting Activity of Catalytic Chain Transfer Agents

In addition to the configuration of the catalyst itself there are other factors that effect the activity of a catalyst within a given system. Simple addition of solvent to a system may cause a decrease in the apparent *Cs* due to competition between monomer, solvent and propagating chains for reaction at the cobalt centre. For example, CCTP carried out in methanol, a strong co-ordinating solvent, significantly reduces catalyst performance[41]. Haddleton *et al.* reported a *Cs* value for bulk polymerisation of MMA in the presence of CoBF as 40000, under identical conditions with methanol this was reduced to 10000. Solvents have been shown to have an effect upon the *Cs* of a system beyond that predicted by simple dilution of the system. Haddleton *et al.* reported that purification by distillation of butanone, removing trace acids, has a dramatic effect on the *Cs* of the system. The *Cs* of CoBF with MMA in untreated butanone was 8020 whereas under identical conditions with distilled butanone a *Cs* of

26500 was recorded[41]. This suggests that trace acids present in solvent cause hydrolysis of the catalyst.

Suddaby *et al.* noted a strange effect when CCTP of MMA and methacrylamide were attempted in dimethlyformamide (DMF) in that no observable polymerisation occurred[46]. DMF is known to co-ordinate to transition metals via the oxygen atom, therefore it is not unlikely that it forms a complex with CoBF[47]. Suddaby *et al.* suggest that the co-ordination of the DMF changes the electronic configuration of the cobalt centre and that this causes the cobalt-hydride to be more stable towards monomer. The increase in stability would mean an increase in competition between hydrogen atom transfer to monomer or the propagating chain. When transfer to a propagating chain occurs it terminates the polymer reducing the concentration of radicals thus inhibiting the polymerisation. As with the CCT mechanism the complex is back to its original form and thus this inhibition is catalytic.

If the proposed mechanism involving co-ordination of the cobalt to the polymer were correct then a change in *Cs* with temperature would be predicted. However this has not been found to be the case in several studies[41,48,49]. Through kinetic analysis Heuts *et al.* drew the conclusion that the rate determining step must be diffusion controlled. The effect caused by an increase in the size of the monomer provides further supporting evidence. Calculation of *Cs* for a series of alkyl methacrylates in bulk has been carried out independently by both Mironychev *et al.* and Heuts *et al.* [49,50]. They found that with an increase in ester chain length a decrease in the *Cs* was observed. This can be partially explained by the increase in propagation rate coefficients as the chain length increases. Mironychev *et al.* provided further explanation and suggested that as a result of increasing steric hindrance with an increase in ester chain length there would be an increase in steric hindrance during the hydrogen abstraction and an

increase in stability of the Co-monomer complex. This would result in a reduction in the concentration of the active species. Heuts *et al.* claim to have evidence to the contrary, as yet unpublished, and ascribe the observation to be consistent with a diffusion-controlled hydrogen-abstraction rate coefficient[49,51].

CCTP has been shown to be most effective for monomers containing an α-methyl group. This was originally explained by the ease of hydrogen abstraction from the α-methyl group compared to abstraction from the polymer backbone. However, studies have shown that the reason lower *Cs* values are observed is due to a reduction in the Co(II) level as a result of the stability of the Co-C bond formed. Heuts *et al.* studied the levels of Co(II) in a mixture of CoPhBF, initiator and monomer, either MMA or styrene[16,52]. After heating at 60 °C for 1 hour and then freezing in liquid nitrogen they obtained electron paramagnetic resonance (EPR) spectra. They noted that in the case of MMA there was no significant difference in levels of Co(II) from those taken before heating. However, in the styrene polymerisation the Co(II) signal had virtually disappeared. They concluded that the reduction in the Co(II) signal was due to the formation of a bond between the styryl radical and the Co(II) complex to form an organocobalt(III) complex, see *figure 1.19*. Earlier studies by Gridnev *et al.* reported similar findings and conclusions through examination of electronic absorption spectra [38,53].

Figure 1.19, Formation of a stable organocobalt(III) complex in the CCTP of styrenics and acrylates

Further evidence is provided by the observation that cobaloximes interact with the propagating chain of acrylates forming a reversible Co-C bond that allows living polymerisation, *section 1.6.2*[54-56].

Co-C bond formation is more significant in the styrene and acrylate polymerisations than with MMA as secondary carbon centred radicals are formed in the case of styrene and acrylates and tertiary radicals in the case of MMA. Firstly tertiary radicals are more stable than secondary and secondly the formation of a bond between an MMA radical and the Co(II) complex is more stericaly hindered than in the case of styrene. Thus for the polymerisation of styrene and acrylates the concentrations of both the propagating radicals and the Co(II) complex would be reduced. A reduction in the level of Co(II) catalyst would mean that the actual ratios of [Co(II)]/[M] are lower than those used to calculate the *Cs*. Heuts *et al.* conclude that the chain transfer rate coefficients for MMA and styrene are probably not as different as the experimentally determined chain transfer constants suggest.

1.5.3 Effect of Catalytic Chain Transfer Agents on Rate of Polymerisation

CCT agents have been shown to cause a reduction in the rate of polymerisation for MMA and styrene. Most of the studies have concluded that this effect is due to chain length dependence of termination, *i.e.* an increase in termination for shorter polymer chains[28,30,57-59].

A further effect of addition of a CCT agent is the postponement of auto acceleration caused by the gel effect until high conversion. This is due to the low molecular weight products formed having a low viscosity[24].

1.5.4 Products of CCTP and their use in Copolymerisation

Catalytic chain transfer polymerisation of methacrylates predominantly yields low molecular weight oligomers. Initiation in CCTP is predominantly by hydrogen transfer from cobalt hydride with termination occurring from β-H abstraction by the cobalt catalyst to yield polymer with an ω-unsaturated end group, *figure 1.20.*

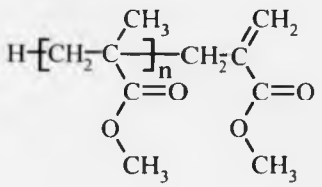


Figure 1.20, Structure of the product of polymerisation of MMA in the presence of a CCTA

These macromolecules can be re-initiated and continue to polymerise, as such they are called macromonomers or macromers. The reactivity of the vinyl bonds in these macromonomers has been found to be between 40-60 % as reactive as the vinyl bond of MMA[60]. The copolymerisation of these macromonomers may result in either the production of block or graft copolymers. Initially reaction of the macromonomer with a propagating chain forms a radical, as shown for a PMMA macromonomer below, *figure 1.21.*

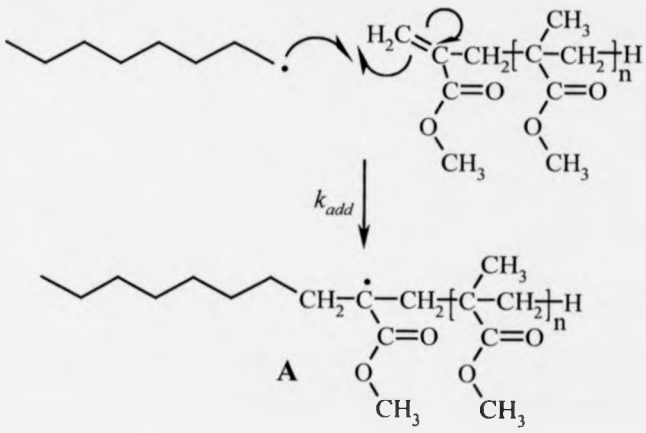


Figure 1.21, Reaction of a PMMA macromonomer with a propagating chain

At this stage there are two possible reaction paths, the first being conventional propagation. This is identical to the copolymerisation of two simple monomers with the copolymer formed having the configuration of a graft copolymer where the macromonomer chains hang away from the polymer backbone as in *figure 1.22*.

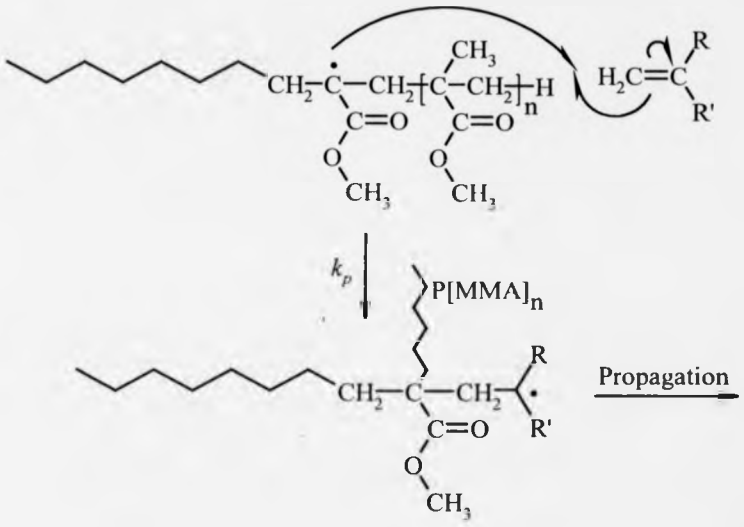


Figure 1.22, Formation of graft copolymers via the macromonomer method

It has been shown that in the absence of monomer the macro-radical **A** (*figure 1.21*) will not undergo termination by combination nor disproportionation to any significant extent due to steric crowding[61]. Instead this hindered radical undergoes β-scission as discussed for chain transfer via an addition-fragmentation mechanism, *section 1.4.2 b*. The result is the production of a new macro radical, which in the presence of monomer will propagate to form a block copolymer. This β-scission pathway is demonstrated for the macro radical **A** below, *figure 1.23*.

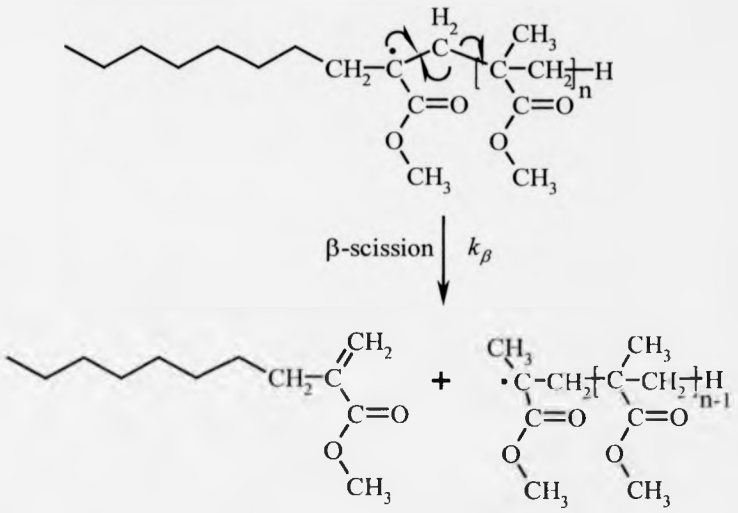


Figure 1.23, Addition-fragmentation of macromonomers produced by CCTP

The relative ratio of propagation : β-scission is largely dependent upon both the comonomer and polymerisation conditions. With monosubstituted alkenes such as acrylates and styrenics studies have shown that formation of graft copolymers is predominant[61-63]. However, a substantial reduction in molecular weight of the copolymers, as compared to the homopolymer, is observed. This can be explained by considering that steric crowding of the radical (**A**) will reduce the rate of propagation so that to some degree β-scission will occur causing a reduction in molecular weight. For polymerisations with disubstituted alkenes, *i.e.* methacrylates, is has been shown that β-scission is the main mode of termination[60,62,64,65]. This is due to increased steric crowding and the lower rate of propagation of methacrylates compared to acrylates, this has the effect of increasing the ratio of the rate of fragmentation to the rate of propagation[60]. The result is that the copolymers formed are predominantly block copolymers.

1.5.5 Summary of Catalytic Chain Transfer Polymerisation

Catalytic chain transfer polymerisation is most efficient for bulk and solution polymerisations of methacrylate monomers. However, the efficiency of CCT agents in the reduction of molecular weight for styrenics and acrylates whilst significantly less than for methacrylates is far superior to the conventional methods of chain transfer agents and increased initiator concentrations. The cobalt complexes also offer benefits beyond their high efficiency in terms of product purity and cost. The catalysts can also be employed in emulsion and suspension polymerisations and whilst activity is greatly reduced in these systems it is found to be 2 orders of magnitude greater than for mercaptan chain transfer agents[42,66].

CCTP lends itself to the production of high purity polymers as only ppm levels of catalyst are required and polymerisations carried out in bulk reach 100% conversion without the problems of the gel effect. Other applications include the use of the ω-unsaturated products for the production of well-defined block and graft copolymers and also as chain transfer agents in the emulsion and suspension polymerisations of acrylic monomers[67,68].

1.6 Living Polymerisation

The subject of living chain growth polymerisation was mentioned briefly in the general introduction, *section 1*, here we discuss the subject in greater detail focussing on transition metal mediated living radical polymerisations (TMM-LRP). Living polymerisation occurs when the reaction is absent of any permanent chain-stopping reactions (*i.e.* chain transfer and termination). If initiation is fast with respect to

propagation then all chains will grow at the same rate until all the monomer is consumed. This means that molecular weight will increase linearly with conversion. Assuming that all the initiator goes on to produce polymer then the degree of polymerisation, DP_n, can be given by the initial ratio of monomer to initiator multiplied by conversion, *equation 20.*

$$DP_n = \frac{[M]_0}{[I]_0} \times \text{conversion} \qquad (20)$$

Where $[M]_0$ is the number of moles of monomer in the feed and $[I]_0$ the number of moles of initiator. The *Mn* of the polymer can be obtained by multiplying the DP_n by the molecular mass of the monomer. A living system will provide a linear relationship between conversion and molecular weight. For systems in which the rate of initiation is very fast with respect to propagation it is assumed that all initiation will occur simultaneously. Propagation occurs at the same rate for all polymer chains and so the polymer is found to have a low polydispersity approaching 1.

Systems with fast initiation and no termination proceed as a pseudo-first-order reaction that can be expressed by the following *equation 21.*

$$\ln\left\{\frac{[M]_o}{[M]_t}\right\} \approx kp[P^*]_t \qquad (21)$$

Through plotting ln $\{[M]_o/[M]_t\}$ vs. time a linear relationship shows that the polymerisation is free of termination, however it does not give us information concerning chain transfer processes. Only through the evaluation of the polydispersity index can the absence of chain transfer be determined. Not only do living polymerisations provide a convenient method for controlling molecular weight and polydispersity but as the polymer chain never terminates once monomer is consumed

the addition of a second monomer will result in the production of a well defined block copolymer.

1.6.1 Ionic Polymerisation

The first living polymerisation system was an ionic polymerisation reported by Szwarc in the 1950s[69]. Both cationic and anionic polymerisations have been described in which the initiating and therefore propagating species is an ion with an associated counter ion. The mechanism of ionic polymerisation contains similar steps to those in free radical polymerisation except termination cannot occur by bimolecular interaction of propagating chains, instead termination occurs by transfer of an ion from solvent or impurity present. Therefore, by purification of reactants and careful choice of solvent permanent chain-stopping reactions are eliminated and the polymerisation is living. However, the need for extremely pure reaction conditions has reduced its industrial use so research has concentrated upon developing techniques to allow living polymerisations through a radical mechanism.

1.6.2 Living Radical Polymerisation

There are three principal mechanisms that have been put forward to achieve living free radical polymerisation. The first is polymerisation with reversible termination by coupling. The first reported system used organosulfur compounds such as $R_2NC(S)SSC(S)NR_2$ (R=Et, Ph), the dormant species formed being $C–SC(S)NR_2$ which is photochemically or thermally activated to allow propagation[70]. This system has been shown to work for both styrene and methyl methacrylate with an increase in

molecular weight with conversion, however polydispersity indices were > 1.5 suggesting that permanent chain-stopping reactions occur to some degree, *figure 1.24* **A**. Another example is the use of the cobaloximes or porphyrins used for CCTP described in *section 1.5.1.* When applied to acrylate polymerisations instead of catalysing chain transfer they tend to inhibit the reaction due to formation of a stable C-Co bond[54,71]. This bond has been found to be labile when irradiated with UV light forming an equilibrium between the dormant species and free radicals, *figure 1.24* **B**. Polymerisations have been shown to be living as an increase in molecular weight with time was observed and resultant polymers had low polydispersity indices (PDI ~1.2). The polymer products were able to undergo subsequent monomer addition presenting further evidence of a living polymerisation system[56].

A better known example is alkoxyamine-initiated or nitroxide-mediated polymerisation as first described by Rizzardo *et al.*[72,73]. This technique employs a stable free radical such as 2,2,6,6-tetramethylpiperidinyloxy (TEMPO). The system is initiated with benzoyl peroxide and the propagating chain forms a dormant species with the TEMPO radical (C—ON), *figure 1.24* **C** [74,75]. There is a fast equilibrium, thermally activated, between the dormant species and the active free radicals, which allows propagation. An increase in molecular weight with conversion is observed and for styrene narrow molecular weight distributions are typical (PDI~1.2)[76]. When this method is applied to the polymerisation of acrylates broader molecular weight distributions are produced suggesting less control than with styrene[73]. Other systems have been investigated with varying success, for example the use of 1-octyl-9-borabicyclononane exhibits some living characteristics, however polydispersity indices are high (PDI~2.5).

The second mechanism for achieving living character is free radical polymerisation with reversible chain transfer. One such example is polymerisation in the presence of alkyl iodides. The propagating chains react with the iodides to form a C-I bond that can be homolytically cleaved, *figure 1.24* **D**. Molecular weight is determined by the ratio of monomer to the iodide and molecular weight distributions are reasonably narrow (PDI~1.3)[77]. More recently the CSIRO (commonwealth scientific and industrial research organisation) reported a living free radical polymerisation based on reversible addition-fragmentation chain transfer which they named the RAFT process, *figure 1.24* **E**[78]. This technique has been shown to be applicable to a wide range of monomers and reaction conditions producing controlled molecular weights and polydispersity indices typically < 1.2[79,80].

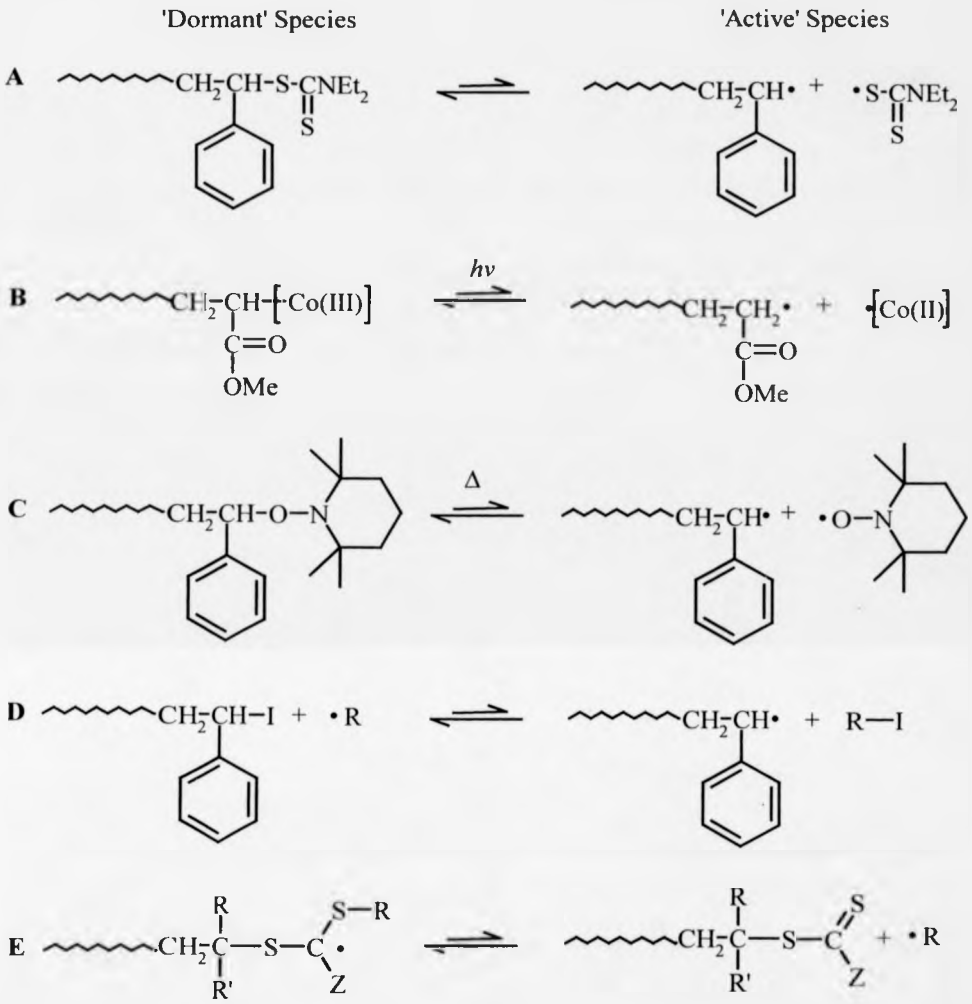


Figure 1.24, Examples of living free radical polymerisations (A) iniferter, (B) CCTP, (C) nitroxide mediated, (D) degenerative transfer, (E) RAFT

The third mechanism is that of transition metal mediated living radical polymerisation which will be discussed in some detail in the following section.

1.6.3 Transition Metal Mediated Living Radical Polymerisation

1.6.3.1 Atom Transfer Radical Addition

In the 1940's Kharasch reported the addition of carbon halogen compounds across a double bond using a catalytic amount of free radical initiator[81]. Reaction of the free radical initiator with the alkyl halide initiates a chain reaction as described by *figure 1.25*.

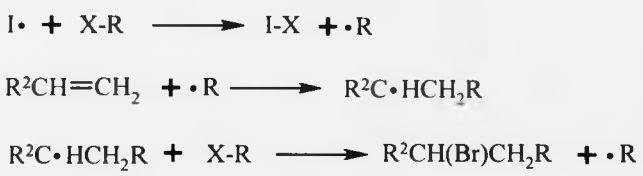


Figure 1.25, The Kharasch reaction

These halogen addition reactions have been investigated extensively and since termed halogen atom transfer radical addition (ATRA). Various methods have been reported for the addition of carbon halide compounds across an unsaturated bond, many of which involve the use of transition metal salts or complexes as promoters[82,83]. The mechanism for these transition metal mediated ATRA reactions is not fully understood. It is postulated that the transition metal complex (M^nX^m) facilitates a rapidly reversible halogen abstraction to produce the free radical, which may then react with the double bond and metal complex $M^{n+1}X^{m+1}$. The resulting product is then trapped by the metal complex ($M^{n+1}X^{m+1}$) to yield the desired product and the original metal complex.

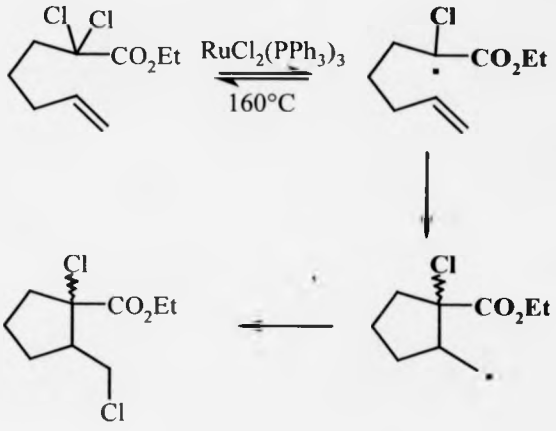


Figure 1.26, Example of an ATRA reaction

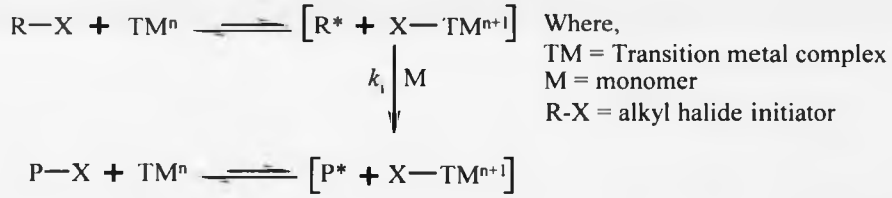
In the example above the first radical centre formed is stabilised by both the chlorine and the ester group which aids the abstraction of the tertiary chlorine, *figure 1.26.* The second radical centre has no stabilisation so once the primary carbon chlorine bond is formed abstraction by the ruthenium complex is not possible.

1.6.3.2 Ruthenium Mediated Living Radical Polymerisation

In 1994 Sawamoto realised the potential of applying ATRA techniques to free radical polymerisations[84]. If the product carbon-chlorine bond could be activated polymerisation would occur by consecutive ATRA steps. The system investigated employed carbon tetrachloride as initiator for polymerisation of MMA catalysed by dichlorotris(triphenylphosphine)ruthenium(II) [$RuCl_2(PPh_3)_3$] and methylaluminum bis-(2,6-di-*tert*-butylphenoxide) [$MeAl(ODBP)_2$]. It should be noted that this and the ATRA systems are heterogeneous. In analogy to the ATRA transition metal catalysed systems the ruthenium complex activates the carbon tetrachloride so that one of the

carbon chlorine bonds is labile facilitating monomer addition. The ruthenium complex may also activate the carbon-chlorine terminal bond formed allowing further monomer additions. Due to the rapid equilibrium between activated and deactivated species undesirable chain transfer and termination reactions are reduced, the result is a pseudo living radical polymerisation. Sawamoto named this transition metal mediated living radical polymerisation (TMM-LRP) but due to its distinct similarities to ATRA is often referred to as atom transfer radical polymerisation, ATRP. The mechanism for transition metal mediated living radical polymerisation is best summarised by the following scheme, *figure 1.27*.

Initiation



Propagation

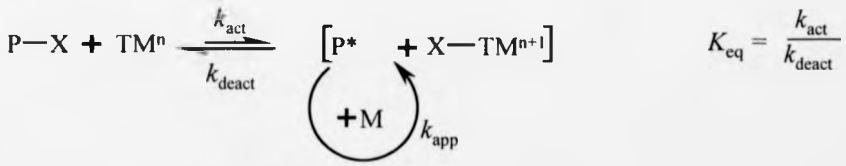


Figure 1.27, Proposed mechanism for transition metal mediated living radical polymerisation

Initially the aluminium compound was not employed resulting in single monomer addition as the ruthenium compound was not capable of activating the CCl_3-MMA-Cl adduct. This limits the range of solvents and functional monomers that this system can

be applied to due to reactions with the aluminium co-catalyst. It is proposed that the aluminium compound co-ordinates to the carbonyl group at the polymer terminal weakening the carbon-chlorine bond sufficiently for the ruthenium catalyst to activate the C-Cl bond. Equally it may be co-ordination to the monomer activating the double bond facilitating propagation or alternatively the aluminium compound may induce ligand exchange with the ruthenium compound to form a more powerful complex. The results of the polymerisation with this ternary initiating system at 60 °C showed that molecular weight increased with conversion and the first order rate plot is linear. 90 % conversion was reached in 4 hours and the polydispersity indexes of the polymers were narrow (PDI ~1.35). After complete monomer consumption a further charge of monomer was added and molecular weights again increased with conversion. All these experiments support that this polymerisation should be called a living system.

In the same paper Sawamoto reports evidence for a radical mechanism. Addition of a stable free radical, galvinoxyl or 1,1-diphenyl-2-picrylhydrazyl (DPPH), caused inhibition and addition of these compounds to an ongoing polymerisation caused immediate termination. An examination of tacticity showed that they had very similar steric structure to those prepared by conventional free radical polymerisation, indicating that the metal complex does not interact with monomer.

Sawamoto has shown that for this system other aluminium alkoxides can be used of which aluminium tri-*iso*-propoxide [$Al(O\textit{i}Pr)_3$] was found to be the most effective and hence the most commonly implemented[85]. There has been examination of many different initiators, all facilitating living polymerisations producing polymers with low polydispersity indices in the range 1.1-1.4, dependent upon initiator functionality and temperature. Ethyl-2-bromoisobutyrate, 2,3-dichloropropionyl chloride,

2,2-dichloroacetophenone, sulphonyl chlorides (RSO_2Cl) and many di and tri-functional initiators have all been shown to be efficient initiators in this system[85-87].

1.6.3.3 Copper Mediated Living Radical Polymerisation

At the same time that Sawamoto was developing ruthenium based chemistry Matyjaszewski was independently investigating copper mediated systems. Using 1-phenylethylchloride, CuCl and 2,2'-bipyridine, styrene was successfully polymerised reaching 95 % conversion in 3 hours at 130 °C[88]. *Mn* increased linearly with conversion, narrow molecular weight distributions were observed and first order rate plots were linear, indicating a living process. This system was also successful for methyl acrylate (MA) and MMA. As with Sawamoto's system it was found that tacticity was identical to that of polymers produced by conventional free radical polymerisation and the stable free radical galvinoxyl inhibited the reaction[89]. Matyjaszewski proposed a mechanism similar to that of Sawamoto again based upon previous research into ATRA reactions.

1.6.3.4 Further Research into Transition Metal Mediated Living Radical Polymerisations

Since the original discovery of TMM-LRP many groups have investigated the efficiency of a variety of transition metal complexes and alkyl halide initiators. The efficiency of the system is dependent upon the equilibrium between active and dormant species. When simple alkyl halides are employed such as butyl chloride and dichloromethane the polymerisations are uncontrolled and polymers with broad

molecular weight distributions are produced. This is due to the high bond dissociation energy of these simple alkyl halides. The high bond dissociation energy means that the formation of a radical is more difficult and therefore a slower process increasing the time span of initiation and thus the molecular weight distribution. Efficient TMM-LRP initiators need to contain inductive or resonance stabilising substituents to weaken the carbon halogen bond. The effect of the halide leaving group is also very significant due to their relative bond strengths. Chlorine and bromine are the only useful halogens with the carbon-bromine bond being the weaker and thus producing a faster polymerisation and narrower molecular weight distributions. Some examples of TMM-LRP initiators that have been shown to produce well-defined polymers are displayed in *figure 1.28*.

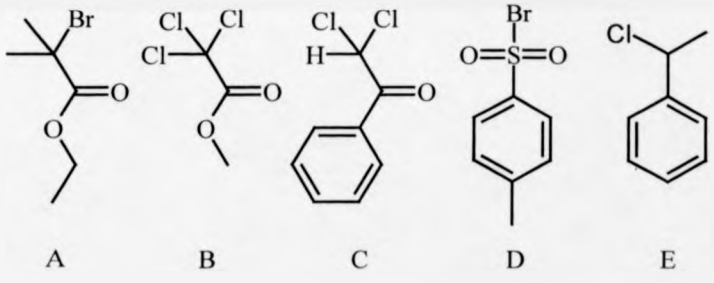


Figure 1.28, Initiators employed in TMM-LRP

Copper(I) halides are very insoluble in organic solvents and monomers and therefore the polymerisation media. Matyjaszewski and Haddleton have explained the role of the 2,2'-bipyridine (bipy) ligand as co-ordinating to the Cu(I) forming a pseudo-tetrahedral $Cu(bpy)_2^+$ complex which is more soluble in organic media[90,91]. The ligand π^* orbitals accept electron density thereby stabilising the low oxidation state of the metal centre. It is considered that when the $Cu(bpy)_2^+$ complex abstracts a halogen atom during the polymerisation oxidation occurs to Cu(II) forming a pentaco-ordinate

species. This would involve rotation of the bipy ligands away from the tetrahedral formation to a distorted square based pyramidal complex. Therefore it has been proposed that a successful ligand for TMM-LRP must increase solubility of the Cu(I)/Cu(II) in the reaction media and be able to switch between the two conformations.

Matyjaszewski has conducted polymerisations concentrating on ligands based upon 2,2'-bipyridine, *figure 1.29* **A** (R=H). Bipy does not completely solubilise the copper(I) halide and the system is heterogeneous and therefore the actual concentration of active species is impossible to determine. However if alkyl chains are introduced to the ligand the copper complex becomes more soluble in the reaction media resulting in homogenous polymerisation systems, such ligands include 4,4'-di-tert-butyl and 4,4'-di-(5nonyl) –2,2'dipyridyl. It was observed that the increased solubility of the catalyst during polymerisation resulted in narrower molecular weight distribution polymers for both styrene and MA (PDI~1.05)[92].

Two similar classes of ligands, N-alkyl-2-pyridylmethylimines (*figure 1.29*, **B**) and 1,4-diaza-1,3-butadienes (*figure 1.29*, **C**), have been shown to be more efficient at accepting electron density into a π^* orbital and therefore more capable of stabilising metals in low oxidation states than bipy [93,94].

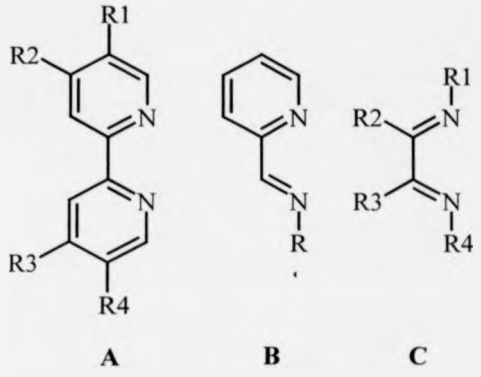


Figure 1.29, Ligands used in TMM-LRP by Matyjaszewski (**A**) and Haddleton (**B**, **C**)

Haddleton has reported the use of N-alkyl-2-pyridylmethylimine copper complexes as efficient catalysts for TMM-LRP[90,95]. However, the 1,4-diaza-1,3-butadienes have yet to be optimised for their use as efficient TMM-LRP catalysts. By altering the inductive effect of the substituent it should be possible to control stabilisation of Cu(I) and Cu(II) and solubility of the catalyst. Initial studies by Haddleton have shown that an increase in chain length of the substituent, whilst increasing solubility in non-polar solvent, has little or no effect upon rate of polymerisation. From the ligands studied, R= Et, *n*-Pr, *n*-Bu, *n*-Pen, *n*-Hex or *n*-Oct there was only any change in rate with the ethyl ligand. Polymerisation with the ethyl system is heterogeneous and it is suspected that the solubility of the Cu(II) complex is even less than the Cu(I) complex. Therefore there would be a decrease in concentration of the deactivator with respect to the activator resulting in an increase in rate of polymerisation as observed. Introduction of branching at the carbon atom α to the imine resulted in a decrease in the rate of polymerisation and an increase in polydispersity index. These two factors are contradictory as an increase in polydispersity suggests an increase in termination.

A decrease in rate is indicative of a lower concentration of radicals and hence reduced rate of termination.

Haddleton has also investigated the effect of addition of substituted phenols that act as radical inhibitors[96]. Whilst more effective in the presence of oxygen they still inhibit reactions via transfer of a phenolic hydrogen atom[1]. The radical inhibitors did not retard the polymerisations as would be predicted if the postulated free radical mechanism were correct, instead there was an increase in the rate of polymerisation. It was found that even in concentrations of 10:1 (inhibitor: initiator) polymerisations lead to polymer with low polydispersity index with *Mn* increasing linearly with conversion. Haddleton has proposed that the postulated mechanism is too simplistic and does not account for all the observations discussed. Instead he offers an explanation involving co-ordination of the copper(I) to the alkyl bromide, weakening the carbon-bromine bond and allowing single electron nucleophilic attack on monomer resulting in the transfer of a bromine atom.

Besides the ruthenium and copper systems many other metal centres have been investigated with varying degrees of success some of the more successful ones are discussed. Sawamoto has demonstrated that $NiCl_2(PPh_3)_2$, $NiBr_2(P\textit{n}\text{-}Bu_3)_2$, $ReO_2I(PPh_3)_2$ and $FeCl_2(PPh_3)_2$ can all be used as TMM-LRP catalysts to produce polymer with narrow molecular weight distributions (PDI < 1.5) when used in conjunction with appropriate alkyl halides, monomers and reaction conditions[97-100]. Teyssié has reported the polymerisation of MMA using a [Ni{$C_6H_3(CH_2NMe_2)_2$-o,o'-}Br] complex / alkyl halide initiating system to possess living character and produce polymers with narrow molecular weight distributions (PDI<1.3)[101]. Percec and Teyssié have independently employed the Wilkinson catalyst, $RhCl(PPh_3)_3$, in the

polymerisation of styrene and MMA respectively[102,103]. The experimental data from these polymerisations are consistent with that of a living polymerisation.

The wide range of metal complexes discussed aid to demonstrate the great versatility of transition metal mediated living radical polymerisation.

1.6.3.5 Persistent Radical Effect

As with any 'living' polymerisation it is assumed that initiation is efficient and fast with respect to propagation, and that termination and chain transfer reactions are negligible. It has been demonstrated that $\ln([M]_0/[M])$ vs. time shows a linear relationship which indicates that the concentration of radicals during the polymerisation remains constant. Therefore from the propagation step in *figure 1.27* the following rate laws can be derived, *equations 22 & 23*:

$$K_{eq} = \frac{k_{act}}{k_{deact}} = \frac{[P^*][Cu(II)X_2]}{[PX][Cu(I)]} \qquad \textbf{(22)}$$

$$R_p = k_{app}[M] = k_p[P^*][M] = k_p K_{eq}[\ln]\frac{[Cu(I)]}{[Cu(II)X_2]}[M] \qquad \textbf{(23)}$$

Equation 23 shows that the rate of polymerisation should be first order with respect to monomer, initiator and copper complex, this has been confirmed by several studies[104,105]. A plot of $\ln(k_{app})$ vs. $[Cu(II)X_2]$ should be linear with a slope of -1 however, this is not observed and at concentrations below 10% of Cu(II) with respect to concentration of Cu(I), k_{app} is not affected. This is explained by considering the concentrations of Cu(I)/Cu(II) in the early stages of a polymerisation. Initially concentrations of active species and Cu(II) are zero. As Cu(I) reacts with the alkyl

halide the concentrations of active species and Cu(II) increase. When deactivating Cu(II) concentrations are low the rate of deactivation is far slower than the rate of termination. As termination occurs the concentration of Cu(II) gradually increases decreasing the concentration of active species until an equilibrium is met and termination reactions are insignificant. When this equilibrium is reached living polymerisation starts to occur. This set of events, termed 'persistent radical effect', was first applied to organic radical reactions by Fischer[106].

1.6.3.6 Summary of TMM-LRP

Whilst TMM-LRP has many advantages there are also some draw backs, the main factor being toxicity of the alkyl halide and often the catalysts employed. Many of the catalysts are also highly coloured with removal being no trivial procedure. Oxidation of the catalyst by the air can be problematic, therefore deoxygenation of solvents, monomers and apparatus and subsequent handling under an inert atmosphere is required. It is interesting to note that Matyjaszewski has reported TMM-LRP using Cu(I)Br in the presence of air. These results showed that whilst Cu(I) was oxidised to the inhibitor Cu(II) providing a sufficient concentration of Cu(0) was added the polymerisation proceeded unhindered after an initial induction period. The induction period is due to the consumption of oxygen present and the establishment of an equilibrium between Cu(II)/Cu(0) to Cu(I).

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Chapter 2

An Introduction to Contact Lens Design

2 An Introduction to Contact Lens Design

This thesis investigates the application of new polymerisation techniques to the polymerisation of functional monomers, mainly methacrylates, of interest to the biomedical industry with emphasise on polymers of interest to contact lens design. Examining the criteria required to produce a successful contact lens reveals many challenges that need to be overcome.

2.1 Requirements of the Eye

Contact lenses can be thought of as an extension of the cornea which they cover; and as such it is important to examine the properties and needs of the eye when considering the design of the lens. The following diagram of the eye has been included for reference during some of the following discussions, *figure 2.1*.

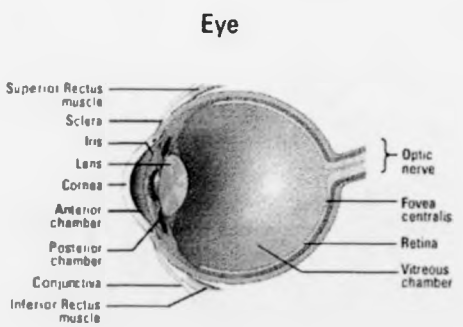

Figure 2.1, Diagram of the eye

2.1.1 The Cornea and Oxygen Permeability

The cornea consists of a gel with a water content of approximately 81 %; the vitreous humour which fills the interior of the eye is also a gel. The cornea contains an insufficient quantity of blood vessels and therefore must obtain its oxygen supply directly from the atmosphere requiring between 3.5 – 7 $x10^{-6}$ $dm^3.cm^{-2}.h^{-1}$. Any material placed over the eye will therefore starve the cornea of oxygen causing corneal oedema, swelling and clouding of the cornea caused by a build up of lactic acid. In severe cases oedema can lead to corneal ulcers, microcysts and inflammation which can all lead to infection and irreparable damage to the eye; it is therefore imperative that contact lenses allow oxygen transport to the eye[1]. Corneal ulcers are formed by a variety of bacteria the most common and dangerous of which is Pseudomonas aeruginosa. In a series of tests by Ren *et al.* it was found that there was a direct relationship between the binding of this bacteria to the human corneal epithelial cells and the oxygen permeability of the contact lens in use. The extent of adhesion is reduced proportionally as oxygen transmissibility increases and lens type was shown to have little effect upon binding of the bacteria[2]. Oxygen permeability (DK) is related to the properties of the material, the actual amount of oxygen reaching the cornea is the oxygen transmissibility (DK/L) and is inversely proportional to the lens thickness (L). It has been estimated that for a contact lens 0.1 mm thick (conventional thickness of a lens) a DK > 100 Barrers is required to meet the cornea's oxygen requirement.

2.1.2 The Tear Film and Wettability

The eye is covered by a tear film that consists of a mucus with a lipid layer on the surface which protects the eye from the atmosphere by limiting evaporation, preventing infection and also providing a route for oxygen supply by osmosis. Any disturbance to the tear film will cause an increase in evaporation and therefore discomfort and possibly irritation. Contact lenses are generally about 10 times as thick as the tear film yet they sit underneath the lipid layer surrounded by the mucus of this film. Wetting of the lens by the tear fluid is essential as it enables a continuous tear film to be maintained on the lens.

2.1.3 Biocompatibility

Biocompatibility is the ability of a material's to perform with an appropriate host response in a specific application and is of great importance in contact lens design. Within the mucus of the tear film there are many biomolecules with many functions including repair of the eye surface and prevention of infection. Biocompatibility of a lens is dependant on the materials bulk and surface properties and their interaction with the biomolecules. Problems associated with biocompatibility are due to deposition of proteins and other tear fluid debris on the lens surface[3]. Deposits can affect material wetting, comfort, visual acuity and may even cause inflammatory responses, often a discolouration of the lens is observed.

2.1.4 Other Considerations

Besides the three main factors discussed, *viz.* oxygen permeability, wettability and biocompatibility, other key issues must be considered. During the blink cycle pressure is exerted upon the contact lens, it must resist the deforming force of the eyelid in order to maintain visual stability, the pressure can also cause displacement of the lens. Therefore the lens must have good mechanical strength but this is normally more important for handling, processing and durability. The lens must also be chemically and thermally stable and obviously, it is imperative that it is optically transparent.

2.1.5 Summary

There are many different types of lenses commercially available which fulfil to varying degrees some or all of the requirements mentioned. The aim of any contact lens manufacturer is to produce a lens which sufficiently overcomes all the problems discussed. This lens would provide optimum comfort and could be worn for extended periods without removal for either the needs of the eye or cleaning purposes. At present, no lens material can fulfil all these requirements though current research may provide the solution.

2.2 Hard Contact Lenses

2.2.1 Original Hard Contact Lenses

The first contact lenses to be made of plastic were designed in 1948 by Kevin Tuohey and were based on poly(methyl methacrylate) PMMA; a newly discovered polymer[4]. The lenses were formed from MMA (~95 %) and a poly vinyl functional compound, or cross-linking agent, which when polymerised forms a vast polymer network. MMA was chosen due to its high modulus of elasticity (required for stable optics), acceptable surface wettability, excellent optical properties, stability, ease of processing, cost and excellent durability. PMMA is also fairly resistant to deposits from the tear fluid although not biocompatible. However, PMMA is practically impervious to oxygen (DK < 0.5 Barrers). This is overcome to a minimal extent by designing the lens in such a way as to permit a good flow of tear fluid to the cornea. Thus enabling a supply of oxygen that is sufficient to allow short term wear for up to ten hours. Many other thermoplastics have been patented for use in hard contact lens application that are more oxygen permeable than PMMA. These include poly(vinyl chloride), cellulose acetate butyrate, polystyrene, poly(4-methyl pent-1-ene) and other halogenated vinyl polymers. However, none of these materials are wettable by the tear fluid and as homopolymers they are redundant in contact lens design. Poly(4-methyl pent-1-ene) is the only material of the polymers mentioned that offers any real benefit over PMMA and that is a significantly higher oxygen permeability (DK ~50 Barrers) and being less rigid and less brittle it is more suited to use as a contact lens material. The significant drawback is that the material is not wettable without surface treatment. Modification of lens surfaces to increase wettability and comfort has been

investigated with positive results however this method is also associated with problems of lack of surface permanence and reduction in surface quality.

2.2.2 Hard Gas Permeable Contact Lenses

To increase oxygen transmissibility of the lens polymers with higher oxygen permeability were examined. The majority of those with suitable properties tend to have the key problem of poor shape memory. Silicon polymers are an exception to this in that they tend to have good mechanical strength. However, these materials are extremely hydrophobic and so not wettable by the tear film and optical studies have shown that they can stick to the cornea[5]. Therefore, in order to produce a hard lens with increased oxygen permeability it is necessary to use these materials in conjunction with other monomers such as MMA. The first commercial gas permeable lens was based on a material developed by Norman Gaylord in 1975 at Polycon Laboratories[5]. It was based on MMA with a small amount of methacrylic acid to improve wettability and contained tris(trimethylsiloxy)-3-methacryloxy propylsilane (TRIS), *figure 2.2* to improve oxygen transmissibility.

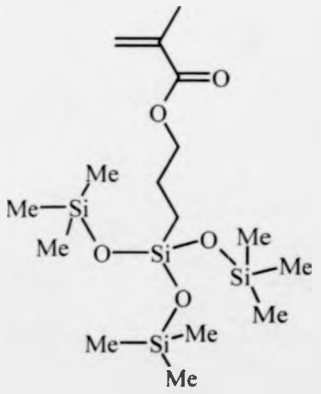

Figure 2.2, Structure of tris(trimethylsiloxy)-3-methacryloxy propylsilane (TRIS)

The lens had a high modulus of elasticity, good scratch resistance, wettability and oxygen permeability. TRIS is still the most commonly used comonomer for improving oxygen permeability in hard lenses mainly because of the high oxygen permeability (DK > 200 Barrers) of the material which is due to the open structure and long Si-O-Si bonds[6]. Hard oxygen permeable lenses are of no use for extended wear due to proteinaceous and lipid build up and the associated irritation that this causes. A report by Mizutani *et al.* concluded that the corneal endothelium of long term wearers of hard PMMA based lenses showed morphological changes[7]. The study also concluded that low DK hard gas permeable contact lenses caused morphological changes to the endothelium though no notable changes were observed in long term wearers of high DK hard gas permeable lenses. It should be noted that materials besides TRIS have been used to improve oxygen permeability. This includes PDMS and its derivatives but also many fluoroalkyl materials, but in this thesis discussion focuses on the use of silicones.

2.3 Soft Contact lenses

Soft contact lenses are at present the only materials to offer the possibility of extended wear lenses primarily due to their greater comfort and associated reduction in irritation. Whilst hard lenses can be shaped to allow tear fluid to flow to the cornea this is not possible with soft lens materials. Therefore, the material itself must allow sufficient oxygen transport to the cornea. Soft contact lenses are split into two types, flexible gas permeable and hydrogel lenses.

2.3.1 Flexible Gas Permeable Contact Lenses

The most obvious choice of material for a flexible gas permeable contact lens was polydimethylsiloxane (PDMS) and derivatives due to their low modulus of elasticity good transparency and excellent oxygen permeability (DK 600 Barrers)[8]. There are several downfalls with lenses of this type in that they are extremely hydrophilic and so not wettable by the tear fluid, they have a high affinity for lipids and they tend to adhere to the cornea. Therefore, lenses of this type are of little commercial interest at present.

2.3.2 Hydrogel Contact Lenses

Hydrogels are polymers that are typically characterised by their hydrophilicity and insolubility in water, whilst having the ability to swell in aqueous medium by the adsorption of water. Their hydrophilicity is due to the presence of water solubilising groups such as –OH, –COOH, $–CONH_2$, –CONH–, $–SO_3H$, *etc* The gel is composed of a cross-linked three-dimensional polymer network that is responsible for its insolubility and stability of shape. There are two main methods of forming hydrogels appropriate to contact lens design. The first is the polymerisation of monomers in the presence of multi vinyl functional compounds known as cross-linking agents. The chains produced by propagation will contain unsaturated cross-linking agent which is capable of further polymerisation. When this occurs the result is the connection of two polymer chains connected by a branch, both chains will contain unsaturated cross-linking agent and so the process is repeated. Eventually the polymers becomes so heavily branched that all the polymer chains are linked to one another through these

branches, the polymer is said to be cross-linked. The second method of hydrogel formation is by using polymers with reactive unsaturated groups (pre-polymers or macromonomers) instead of monomers. It is also possible to use a blend of both monomers and macromonomers. The extent of cross-linking is dependent upon the reactivity of the cross-linking agent with the monomer(s) and concentration. The extent of cross-linking directly effects the equilibrium water content (EWC = the percentage by weight of water in the swollen gel) and strength of the gel, and is therefore an extremely important property. The EWC is also governed by surface tension, pH and ionic strength of the aqueous medium and of course chemical composition. The EWC of a hydrogel can therefore be well controlled by the ratio of hydrophilic and hydrophobic constituent monomers. EWC is a particularly important consideration for contact lenses as both the pH and surface tension of the aqueous medium in which they are placed change from person to person and to a limited extent throughout the day.

2.3.2.1 Features of Simple Hydrogel Lenses

Wichterle and Lim were the first to report the use of lightly cross-linked polymers of 2-hydroxyethyl methacrylate (HEMA) for biomedical applications in the 1950s and 60s[9,10]. In 1961 they developed a method of spin-casting to enable the use of these materials as contact lenses[11]. Hydrogels are a particularly attractive material for contact lenses because they possess excellent optical properties, they are readily wetted by tear fluid and because they are soft they can be moulded to conform to the corneal structure to give greater comfort. Control of the mechanical properties of hydrogels is controlled in several ways. Decreasing EWC, increasing thickness of

lens, adding high Tg comonomers and increasing cross-linker concentration all result in an increase in the strength of the lens. With a hydrogel lens the cornea is supplied with oxygen that is dissolved in the aqueous phase of the gel. As oxygen is used by the cornea it is replenished from the atmosphere, the driving force for this replenishment coming from the chemical potential gradient formed. The amount of oxygen reaching the cornea is dependant on two factors; the first being the quantity of oxygen dissolved in solution and the second being the hydrogels resistance to migration both relying on composition (chemical & structural) and thickness. As the EWC is increased the oxygen transmissibility of the lens is also increased, however there is still an appreciable dependence on the chemical nature of the polymer[12,13]. Poly(HEMA) has a fairly low oxygen permeability (DK=10 Barrers) and typical EWC of 40 % and in its original thickness was of no use as an extended wear material[1]. Ciba-Geigy and Bausch & Lomb have both produced extremely thin lenses in an attempt to overcome this problem, whilst the lenses were a significant improvement over the standard poly(HEMA) lenses they were too weak causing handling difficulties for the user. It has also been shown that in dry environments thin high water content lenses can cause epithelial dehydration which results in damage to the cornea[14]. An alternative approach is to increase the water content of the lens by using different monomers. Incorporating ionic monomers (*i.e.* methacrylic acid (MAA), or acrylic acid (AA)) with less hydrophilic monomers increases the water content of the gel. Copolymers of HEMA with as little as 6 % (w/w) MAA at a pH of 7.4 have a water content of 70 %, an increase of 30 % over the homopolymer of HEMA[6]. However, the biomolecules present in the tear film have a high affinity for ionic species and so this method is not satisfactory due to the excessive deposits formed[15]. An alternative is to use monomers with much higher hydrophilicity than

HEMA such as *N*-vinyl pyrrolidone (NVP), *N,N*-dimethyl acrylamide (DMA), glycerol methacrylate (GM) and zwitterionic monomers such as *N,N*-dimethyl-*N*-methacryloxyethyl-*N*-(3-sulphopropyl)-ammonium-betain (SPE). As a rough guide it has been estimated that an EWC of between 30-50 % for day wear and 70 % for overnight wear for lenses of between 0.15-0.2 mm thickness is required for a sufficient oxygen supply to the cornea. It is easy to obtain lenses with these high water contents in fact copolymers of HEMA with NVP or DMA have water contents ranging from 40 to over 90 %. However, a lens with an EWC of 70 % will have dramatically reduced mechanical stiffness, this can cause visual instability during blinking and poor durability and handling qualities. Making copolymers with hydrophilic monomers that have higher Tg (*e.g.* hydroxypropyl methacrylate or 4-*t*-butyl-2-hydroxycyclohexyl methacrylate) or increasing the extent of cross linking help to overcome mechanical weakness but result in a reduced EWC[16,17]. Increasing the lens thickness will improve mechanical stability but reduce oxygen transmissibility offsetting the effect of increasing the water content. Another draw back associated with increasing water content is the increase in deposition of proteinaceous and other tear fluid debris on the lens[18]. Nevertheless, lenses of these type were approved by the American food and drug administration (FDA) for wear of thirty days without removal. Subsequently this was reduced to seven days due to a significant increase in cases of infections and corneal erosions in users of the hydrogel extended wear lenses.

2.3.3 Silicon Hydrogels

Current research is concentrating on increasing the levels of oxygen permeability by attempting to merge the best properties of hydrogels with silicon lenses. The primary focus is on incorporating silicones into non-ionic hydrogels, however this is not a trivial task due to the incompatibility associated with the hydrophilic nature of monomers used to form hydrogels and the extreme hydrophobic nature of silicones. Simple copolymerisation of hydrophilic monomers with siloxanes (*e g.* methacrylate or vinyl functionalised polydimethylsiloxanes or TRIS) results in hydrogels with good oxygen permeability and variable water content, typically less than 30 %. The drawback being the materials are invariably opaque due to phase separation and so obviously not suitable for contact lens design. It is to be noted that soft contact lenses require a high modulus of elasticity and that incorporation of TRIS and other silicones tends to reduce the modulus of elasticity of the resultant gel. However, it has been found that making gels from low molecular weight macromonomers of TRIS has no effect on the modulus and simply increases the oxygen permeability of the material[19]. It is also beneficial to use lower rather than high molecular weight pre-polymers because it allows for a more random distribution of siloxane groups thus minimising the formation of large incompatible domains.

2.3.3.1 Techniques for Silicon Hydrogel Production

Many methods have emerged which allow production of non-phase separated silicone hydrogel materials however, for most of these there are associated drawbacks. These techniques are now discussed but due to the vast quantity of patents covering this

area, only the key methods are discussed focusing on the original literature and not the simple variations that have arisen.

a) Solvents and Specific Monomer Ratios

The most simplistic technique is the addition of hydrophilic solvents such as isopropanol or hexanol to the formulations which solubilises the incompatible materials. The incorporation of solvent has worked for some monomer systems but is primarily used in conjunction with approaches discussed later.

Many patents cover specific ratios of silicone monomers with hydrophilic monomers that produce optically clear materials. For instance US patent 5786434 describes lenses produced from mixtures of a) either N,N-dialkyl acrylamide or methacrylamide, b) one of several N-vinyllactams (including N-vinyl pyrrolidone and N-vinyl caprolactam) and c) a bis(silicon-containing alkyl) fumurate, *figure 2.3*. Only at specific ratios are transparent materials produced but the patent describes a lens which has excellent oxygen permeability independent of water content, a high mechanical strength and good flexibility[20].

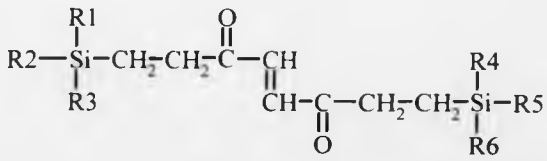

Figure 2.3, Chemical structure of bis(silicon-containing alkyl) fumurates, where R1-6 = alkyl or trimethylsiloxy groups

b) Protection-Deprotection Route

Another approach is the use of protection-deprotection chemistry, in particular the use of trimethylsilyl (TMS) protected HEMA as a comonomer with methacrylate functionalised PDMS. When mixed the two monomers are completely miscible and after cross-linking produce a clear material. The hydroxyl groups are subsequently deprotected by immersing in either an acidic or basic solution followed by purification to remove by-products. The hydrogel formed has good optical properties but this is an expensive approach due to the number of processing steps and time associated with them[21].

c) Hydrophilic Silicon Monomers

The main area of research has been on production of silicon materials with hydrophilic groups making them miscible in hydrophilic monomers. As previously discussed TRIS is an important monomer in the path to high oxygen permeable contact lenses. Gel formation of TRIS with hydrophilic monomers results in phase separated material even when a solvent is used. Tanaka *et al.* demonstrated that through modification of the TRIS monomer to increase hydrophilicity clear hydrogels could be produced. Their approach was the addition of a hydroxyl functionalised spacer between the methacryloyl and silicon groups to produce tris(trimethylsiloxy)silyl propyl glycerol methacrylate (SiGMA, *figure 2.4*). It was shown that SiGMA was fully miscible with HEMA, NVP and DMA without the need of a solvent. A range of hydrogels were produced with water contents between 15 and 50 % all were optically clear and had higher oxygen permeability than non silicon

hydrogels with the same EWC[22]. Similarly, Harvey examined a variety of modified TRIS monomers with additional hydrophilic groups. The most applicable is tris(trimethylsiloxy)silyl propyl methacryloxyethylcarbamate (TSMC) which has the more hydrophilic methacrylamide group in exchange of the methacrylate group of TRIS, *figure 2.4*. This silicone monomer is soluble in hydrophilic monomers, and so copolymers of TSMC with NVP or DMA over a large range of compositions were prepared. These materials had a wide range of mechanical and physical properties. A hydrogel of TSMC with 40 % DMA had a high water content (38 %) was transparent and had a DK of 58 Barrers which is considerably higher than a standard hydrogel with a similar water content[23]. The modification of TRIS monomer has also been demonstrated by Bambury and Seelye. In a similar style to Harvey they replaced the methacrylate with a vinyl carbamate or carbonate. When polymerised with NVP these produced clear gels with high oxygen permeability and good EWC, in some cases a solvent was required to prevent phase separation. As the overall quantity of the hydrophilic monomer was increased an increase in water content and a decrease in oxygen permeability was observed[24]. Lenses made from these materials have been approved for extended wear by the FDA under the trade name balafilcon A for some years. However, due to problems associated with excess lipid and protein deposition and wettability the release of contact lenses produced from this material were severely delayed. Recently Bausch and Lomb released Pure Vision™ a hydrophilic contact lens containing balafilcon A with a high oxygen permeability and EWC. Bausch and Lomb overcame wettability problems by plasma treating the surface of the lenses which produces a thin hydrophilic layer. The lens was designed for extended wear of up to 7 days between removal for cleaning and disinfection or disposal. However, clinical trial of this lens has shown that when compared to the control patients

concluded that the Pure Vision™ lens suffered from higher deposits and discomfort typical of a silicon hydrogel lens[25]. Therefore the study concluded that whilst the lens has many of the required properties of an extended wear lens it only exists to complement the wide range of lenses already available and does not have any considerable benefits.

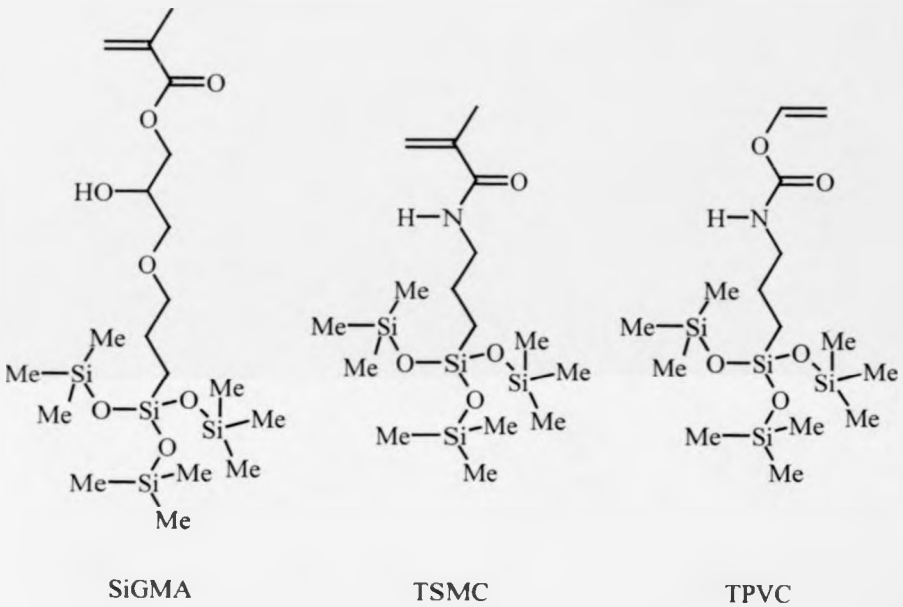

Figure 2.4, Chemical structures of modified TRIS monomers: SiGMA, TSMC and TPVC

d) Siloxanes Containing Hydrophilic Grafts

Another approach is that of modification of PDMS and similar siloxanes by the attachment of hydrophilic grafts which help make the materials soluble in hydrophilic monomers. Keogh *et al.* attached mainly di or triethylene glycol or alcohol hydrophilic units to the backbone of methacrylate end capped polysiloxanes[26]. The

polysiloxane backbone contained Si-H groups and by platinum catalysed hydrosilation di or triethylene glycol allyl methyl ether or allyloxy functionalised trimethylsilyl protected alcohols were attached to form the graft copolymers. A range of polysiloxanes with a vaiety of molecular weights, percentage graft and length of graft were produced. Their properties for hydrogel formulation with a variety of hydrophilic monomers were examined. The results were positive and most combinations provided clear silicon hydrogels without the need of a solvent. The materials were found to have good oxygen permeability and acceptable water contents.

Similarly Künzler *et al.* used hydrosilation to attach fluorinated chains (DP = 4 or 8) to methacrylate end capped PDMS. 10, 25 and 40 % substituted PDMS was investigated with various lengths of fluorinated chains. When the functionalised polysiloxanes were polymerised with hydrophilic monomers transparent, wettable materials were produced with good oxygen permeability providing the $(CF_2)_n$ grafts contained a CF_2H end group and not CF_3. A lens produced from a polysiloxane (DP = 100) with 25 mol % tetra fluoride grafts copolymerised with DMA (40 mol %) had an EWC of 45 % and high oxygen permeability (DK 115 Barrers). Decreasing the DMA content to 20 mol % caused a decrease in hydrophilicity resulting in a decrease in the EWC to 18 % and an increase in the oxygen permeability of the hydrogel to 222 Barrers. Increasing the length of the fluorinated chain has no effect on EWC or oxygen permeability of the materials. All the materials had good modulus of elasticity, tensile strength and tear strength[27,28].

e) Siloxanes containing hydrophilic blocks

Another way to introduce hydrophilicity to the polysiloxanes is the addition of hydrophilic blocks. Su and Robertson have examined the properties of PDMS with polyethylene glycol (PEG) or polypropylene glycol (PPG) blocks. Styryl end capped short chain length PEG and PPG were added to hydride terminated low molecular weight PDMS via platinum catalysed hydrosilation to form di and tri block copolymers with methacrylate functionality. When these materials were copolymerised with HEMA transparent hydrogels were formed with reasonable water content (EWC = 22 %) and high oxygen permeability[29,30]

Similarly Lai prepared methacrylate terminated urethane-PEG-PDMS tri-block copolymers. Through adjusting the various chain lengths of the blocks, copolymers with a wide range of mechanical and physical properties can be produced. When reacted with HEMA or DMA optically clear hydrogels were formed with good water content, wettability and oxygen permeability[31].

f) Silicon Pre-Polymers

Several routes have been described using vinyl functional pre-polymers. Mueller produced several methacrylate functionalised copolymers of TRIS which were found to have good properties for producing silicon hydrogels[32]. The copolymers were produced by free radical polymerisation of TRIS with a hydrophilic monomer, *e.g.* DMA and a small percentage of a hydroxyl or amine functional monomer in the presence of a chain transfer agent. The hydroxyl or amine groups are subsequently reacted with methacryloyl chloride or methacryloxyalkylisocyanates to produce a

copolymer with methacrylate groups distributed along the backbone. These random copolymers were found to have better solubility than homopolymers of TRIS in hydrophilic organics. When polymerised with hydrophilic monomers such as DMA or HEMA to produce hydrogels the materials were found to have satisfactory water contents, acceptable wettability, were transparent and had good oxygen permeability. Mueller has also used this method to produce copolymers of fluorinated and alkyl methacrylates with TRIS for use in lens synthesis[33]. Again, these materials when cross-linked with applicable hydrophilic monomers produced acceptable non-phase separated lenses.

Spinelli demonstrated that group transfer polymerisation could be used to produce blocks of TRIS with DMA using a trimethylsilyl protected hydroxyl functional initiator. Following deprotection the hydroxyl group is reacted with isocyanoethyl methacrylate to give a methacrylate end capped hydrophilic siloxane macromonomer. The macromonomers were homopolymerised as well as being copolymerised with various hydrophilic monomers to produce silicon hydrogels with a wide range of physical and mechanical properties. Among these materials many showed good wettability characteristics, had good oxygen permeability and were optically clear[34]. Spinneli also used this method to produce stars with silicon centres and hydrophilic arms[35]. Anton *et al.* have also produced star copolymers of TRIS with HEMA. The hydroxyl groups of the HEMA were then reacted with isocyanates or glycidyl methacrylate. These methacrylate functional star copolymers were then reacted with hydrophilic monomers to produce silicon hydrogels many of which were transparent[36].

f) Combination of Techniques

Other examples have involved a combination of the techniques already discussed. Lai has shown that TRIS can be used as a compatibiliser between PDMS and DMA[37]. With DMA at 40 % (w/w) by varying the proportions of TRIS and PDMS it is possible to produce clear solutions. With TRIS at concentrations of 47 % (w/w) and higher the small percentage of PDMS (DP = 50) present was miscible with DMA. In the absence of the TRIS the solutions were found to be phase separated. On polymerisation of these solutions with an appropriate cross linker the silicon hydrogels produced were found to be phase separated. This was overcome by using high volumes of solvent (*e.g.* hexanol 40 %), the resultant gels having good wettability, EWC, high oxygen permeability and transparency. However, the high quantities of TRIS cause a significant reduction in the modulus of elasticity of the lens. With lower molecular weight PDMS (DP = 25) less TRIS is required to achieve a compatible mixture. Formulations containing 40 % DMA, 30 % TRIS and 30 % PDMS were miscible. The silicon hydrogels produced from this formulation (with the use of 40 % hexanol) were clear, had a moderate water content (EWC = 29 %), high oxygen permeability (DK = 99 Barrers) and a good tear strength. Lia carried out a similar study using di and tri block polyurethane PDMS copolymers in which the same conclusions were drawn[38].

2.3.4 Summary of Silicon Hydrogels

Several methods have been described for producing silicon hydrogels with a range of EWC, oxygen permeability and mechanical properties. Whilst patents covering silicon

hydrogel lenses continue to emerge they tend to use prior art in the forms discussed simply covering different monomers and macromonomers that are applicable to contact lens design. Many of these patents claim to have discovered materials which are both highly oxygen permeable and wettable however clinical trials have shown that there are some key problems with all the materials mentioned and so not suitable for extended wear. Whilst the materials have been shown to be wettable to water it has been found that many are not sufficiently wettable to the tear fluid. They were also found to have very high lipid deposits. These factors have obvious consequences the major of which is discomfort to the user. The reasons for these problems have been attributed to the tendency of the hydrophobic siloxanes to migrate on hydration to the air surface as it has a lower surface energy, and therefore the surface of the lens has the characteristics of a hard silicone lens[39].

2.3.5 Mould Influences

Lai *et al.* have demonstrated that the polarity of the mould strongly influences the composition of the surface of these silicon hydrogels. They examined a variety of materials that have been patented as suitable silicon hydrogels for contact lens design. When lenses were prepared in hydrophobic polypropylene moulds (PP) they exhibited bad surface properties with extremely poor wettability to the tear fluid and protein build up was severe. In one example the lenses could not be worn for more than an hour before deposits were so heavy that the lens was opaque and caused extreme discomfort due to lack of surface wettability[39]. It is postulated that the hydrophobic silicon materials are drawn towards the hydrophobic mould and so once cured the lens has a surface high in silicon. Attempting to overcome this problem Lai and Friends

examined a polar acrylonitrile copolymer mould (AN) presuming that the more hydrophilic components of the lens formulation would adhere to the surface. They also examined using a combination of PP posterior mould and AN anterior mould. Once cured on hydrating the hydrophobic silicon moieties would be unable to migrate to the lens surface preventing the poor surface properties commonly observed. Lenses produced in an AN mould from the material with the worst results in the PP test, had significantly improved surface properties, however they were still not ideal. Formulations high in hydrophilic monomers and low in siloxanes which formed lenses with high EWC (~50 %) had very good properties when prepared with a mould that had an AN anterior and PP posterior. These lenses had extremely good wettability and relatively low lipid deposits over a short period. Whilst this method of lens manufacture significantly improves the properties of the lenses only lenses low in silicon content have suitable surface properties and thus do not have sufficiently high oxygen permeability to allow extended wear. Neither does the method overcome the problem of lipids depositing into the bulk of the lens from tear fluid diffusing through the lens.

2.4 Biocompatibility and Phosphoryl Choline

As discussed earlier in this chapter it is advantageous if the material of a contact lens is biocompatible so that excess protein and lipid deposits do not develop when worn for an extended period. Infact protein and lipid deposits have been the main problem with the extended wear silicon hydrogel materials discussed. The biocompatibility of a material is governed by the interaction of biomolecules present in the medium in which it will be placed. Because of the diverse nature of the human body a

biomaterial may be biocompatible in one application for a specific purpose, but not in a similar application at a different site. Therefore, in developing a biomaterial the biological environment needs to be examined. For contact lens design it is relevant to examine haemocompatibility studies due to the correlation in biochemical components of the tear film with that of blood.

When alien materials enter the blood stream, several responses from the biological defence system are possible. All involve the initial rapid adsorption of proteins, the type being dependent upon the response of the body's immune system. Primarily adhesion proteins stick to the surface of the alien material and form a base for the subsequent addition of other blood deposits. To understand the mechanism of protein adhesion in this environment it is important to consider the surface properties of the proteins. The surface of a protein is often complex in nature containing large areas of hydrophobicity, hydrophilicity and charge. Therefore there is potential for it to bind to any type of surface and so it is not possible to predict a material which will be biocompatible. However, Andrade hypothesised that materials with even distributions of polar and non polar sites would not be suitable for the binding of proteins [40]. Biological membranes are composed of a fluid lipid bilayer that supports integral and peripheral proteins. The simplest common feature of the outer membrane of blood cells, platelets, lymphocytes and many other biological membranes is the high content of phospholipids[41]. The predominant phospholipids are phosphatidylcholine, phosphatidylethanolamine and phosphatidylserine and sphingomyelin. The lipids consist of a polar head group and long hydrocarbon chains that may be of different lengths with differing degrees of unsaturation. Out of these phospholipids it has been shown that the phosphatidylcholine lipids are the primary cell component responsible

for human cell compatibility. The phosphatidylcholine lipids contain the hydrophilic zwitterionic head group, phosphoryl choline, *figure 2.5*.

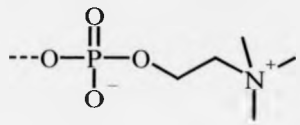

Figure 2.5, Structure of phosphoryl choline

Previously it was mentioned that ionic molecules have a tendency to accumulate protein. Therefore, it may seem strange that the introduction of the ionic phosphoryl choline unit decreases adsorption. This is due to the group being zwitterionic and at physiological pH is electronically neutral. In haemocompatibility studies it has been found that polymers with a strong affinity for phospholipids generally cause deposition of albumin (a collection of small proteins) which forms a biocompatible surface on the object, in the case of contact lenses this film would cause problems with clarity[42,43]. Sevastianov has shown that hydrophilic blood compatible surfaces generally have less lipid and protein deposition than their hydrophobic counterparts[44].

2.4.1 Phosphoryl Choline Polymers for Medical Implants

A considerable amount of research has focused on the production of polymers containing similar functionality to the head group of the phospholipids discussed. Much of this work has been recently reviewed by Nakaya, the article providing a considerable insight into the chemistry employed to make such materials[45]. This report focuses on the use of phosphoryl choline functionalised polymers as biocompatible materials which was first reported by Nobuo Nakabayashi and independently by Dennis Chapman[46]. Chapman reported the effectiveness of

polymers modified to contain the phosphoryl choline group at dramatically reducing protein and lipid deposition in haemocompatibility studies[47-50]. Since the initial findings of Chapman and Nakabayashi there has been great interest in the use of phosphoryl choline functionalised polymers. The phosphoryl choline unit has been incorporated onto a variety of monomers including HEMA to produce the monomer 2-(methacryloxyethyl)-2'-(trimethylammoniumethyl)phosphate (HEMA-PC or MPC), *figure 2.6*[45,51].

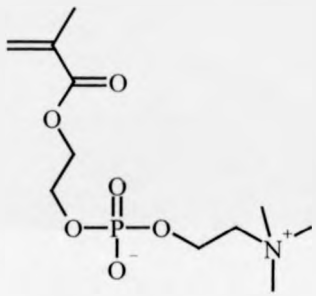

Figure 2.6, Structure of 2-(methacryloxyethyl)-2'-(trimethylammoniumethyl)phosphate (HEMA-PC or MPC)

The production of this monomer has allowed easy synthesis of many phosphoryl choline containing copolymers. There are many papers and patents covering the production and effectiveness of such materials at reducing protein deposition, a few of which are discussed here.

A graft copolymer of HEMA-PC and *n*-butyl methacrylate (*n*-BMA) has been produced by conventional free radical polymerisation. The copolymer has proven to exhibit biocompatibility with much lower platelet adhesion, aggregation and protein adsorption in the presence of human blood compared to other synthetic polymers designed to be biocompatible. A study of copolymers of HEMA-PC with *n*-butyl

methacrylate (*n*-BMA) or lauryl methacrylate (LMA) by Ishihara showed that when placed in whole blood these materials exhibited only low levels of protein deposition. Whilst the LMA copolymers were shown to have less deposits than the *n*-BMA copolymers the difference was minimal. When the same tests were carried out with homopolymers of LMA, *n*-BMA and HEMA there was massive deposition on the materials surfaces[52]. It has also been shown that copolymers of HEMA-PC with various other alkyl methacrylates including hexyl, *t*-butyl and *n*-stearyl and also HEMA all had good biocompatibility in blood[53]. Nakabayashi *et al.* have shown that many copolymers containing HEMA-PC including those of *n*-BMA and styrene are biocompatible and when applied as coatings dramatically decrease platelet adhesion, aggregation, protein adsorption and adhesion. It was also shown that the presence of the phosphoryl choline initiates the adsorption of natural phospholipids onto the polymer surface (confirmed by X-ray photoelectron spectroscopic analysis). Nakabayashi proposed that this lipid layer is responsible for the increased biocompatibility[54-56]. Chapman has developed methods to functionalise the surfaces of materials including PVC, polyethylene, polypropylene, celluloses and polyurethanes with phosphoryl choline the resultant materials having good biocompatibility[57]. These studies show that it is possible to vary comonomer functionality with little or no effect to the biocompatibility of the resultant material. This allows for biocompatible materials with a diverse range of mechanical properties to be produced thus extending the range of applications to which phosphoryl choline technology is applicable. The materials discussed are applicable to medical devices such as intravascular catheters, urethra catheters, hip replacements and heart pacemakers among many other medical implants.

2.4.2 Biocompatible Polymers for Contact Lenses

Whilst it is relevant to examine materials which are found to be biocompatible in haemocompatibility studies there are key differences between the devices these materials were designed for and contact lenses. For example, simple surface coatings suffice for many of the implants discussed whereas this is not possible for soft contact lenses. This is because for a soft contact lens bulk properties are as important as the surface properties due to the flow of tear fluid through lens. Different approaches have been examined for the production of a biocompatible contact lens. The first and probably most efficient is the use of phosphoryl choline technology, other studies have examined the use of polyethylene glycols.

2.4.2.1 Phosphoryl Choline Biocompatible Contact Lenses

To date only one contact lens material is available that uses the phosphoryl choline technology and is licensed under the trade name omafilcon-A. The material is a simple formulation of HEMA and HEMA-PC that is cross-linked to form a lens with an EWC of 59 %. The material is marketed under the name 'Proclear' and more recently, the disposable lens 'Proclear compatibles' was introduced. Approximately 50 % of contact lens wearers suffer from dry eye symptoms that include discomfort, poorer tear film stability and increased ocular surface damage when compared to normal eyes. This is of particular relevance in countries with hot and dry climates where hydrogel lenses are prone to dehydration. The discomfort associated with dry eye has lead to an estimated 35 % of wearers to permanently discontinue the use of contact lenses[58]. It is important to note that the phosphoryl choline group has a

significant affinity for binding water and therefore the water content of this lens is less affected by change in temperature and thus maintains its high oxygen transmissibility. There have been several studies involving Proclear lenses and they have all concluded that there is less on-eye dehydration, superior comfort, lower levels of protein and lipid deposition and less corneal staining (indicating less damage to the eye) with Proclear than a wide range of soft contact lens materials[59-63]. A more recent study by Lemp involving contact lens wearers with symptoms associated with dry eye has shown that by changing over to Proclear that in the majority of cases patients symptoms were alleviated. The study concludes that the biocompatible nature of this lens makes it an ideal choice for patients with mild to moderate dry eye conditions[64]. A similar study to that of Lemp has shown that the disposable Proclear compatibles are equally superior to there competitors[65]. Whilst omafilcon-A has a higher oxygen permeability than other hydrogel contact lenses there is not a sufficient oxygen supply to enable extended wear.

2.4.2.2 Polyethylene Glycol Biocompatible Contact Lenses

Other studies have investigated the use of PEG to reduce tear fluid deposition. Sariri *et al.* examined various copolymers of HEMA/MMA (50:50) with different levels of polyethylene glycol methyl ether methacrylate (MeOPEGMA) or polyethylene glycol methacrylate (PEGMA) of various molecular weights[66]. The copolymers with PEGMA had increased protein deposits whilst those with MeOPEGMA showed significant reduction in protein deposition. It was shown that as the molecular weight of the MeOPEG chains increased there was a lowering in protein deposits. Sariri proposed that the reason for a decrease in protein deposition is that the long PEG

chains are free on the surface of the hydrogel forming a 'carpet' to which the proteins cannot bind. Similar studies by Andrade *et al.* agreed with the study of Sariri and they proposed that the decrease in adsorption observed with PEG is due to the rapid movement of the PEG chains in solution influencing the protein solution surface interface such as to prevent adsorption or adhesion of proteins[67,68].

2.5 Summary

As we have seen the key problems are that of oxygen permeability, wettability, tear fluid deposition and comfort. Contact lenses available at present are a vast improvement over their predecessors however no materials are available that allow the possibility of an extended wear lens for periods exceeding 7 days without increasing levels of serious eye complaints. We have reviewed many ways in which companies have attempted to overcome these problems focusing upon the production of silicone hydrogels as this is the most likely route to success. To quickly review the methods discussed were addition of blending solvents and or monomers, production of more hydrophilic silicon monomers, polysiloxanes with hydrophilic grafts / blocks and silicon pre-polymers.

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Chapter 3

Modification of the ω-Bromo End Group of Polymers Prepared by Copper-Mediated Living Radical Polymerisation to yield Functional Telechelics

3 Modification of the ω-Bromo End Group of Polymers Prepared by Copper-Mediated Living Radical Polymerisation to Yield Functional Telechelics

The α- and ω-end groups of a polymer are dictated by both the methods of initiation and permanent chain stopping reactions, *i.e.* termination and transfer, respectively. Telechelic polymers are defined as having both α- and ω- functional end groups and are of particular interest for post-polymerisation reactions, *i.e.* crosslinking, coupling reactions and/or chain extension. For example telechelic oligomers have been used to produce high solid content coatings that rely on oligomers curing on application. This can be beneficial over conventional pre-formed polymer coatings that are applied dissolved in organic solvents, which raises environmental issues and increases costs. Besides the reactivity aspects of the polymer the end groups can control the stability of the molecules with respect to heat, light and oxidation[1]. They can also cause a change in the physical properties of the polymer such as crystallisation ability, viscosity and mechanical behaviour in general[1,2]. Therefore having control of end functionality enables control of these properties, which can be of benefit to both processing and application.

The use of telechelic polymers commercially has concentrated upon polymers formed through step growth reactions. For example, reaction of a diacid with excess diol leads to α,ω-dihydroxytelechelic oligomers which are used for coating applications and polyurethane foams. The synthesis of telechelic polymers via chain growth polymerisation is less well developed. Anionic polymerisation offers fairly good selectivity over end group functionality. Initiators are selected to control the α-end but

typically this requires the use of protection group chemistry. ω-Functionality is introduced by terminating the polymer with a carbanion, and as a wide variety of functional carbanions are available a wide range of telechelic polymers can be formed[3]. However, anionic polymerisation is not usually industrially applicable, mainly due to costs associated with the stringent reaction conditions and high purity reagents that are required.

A number of methods to produce telechelic polymers by free radical polymerisation have been available for several years. The crudest method is the addition of comonomers that form cleavable weak links in the polymer, however this leads to a variety of products. For monomers that predominantly terminate by combination, using high concentrations of functional initiator will produce a polymer with functionality at both ends[4-6]. This method is unreliable as quantitative analysis of the amount of termination by combination varies from source to source, styrene for instance has been shown to terminate by anywhere between 80 to 100 % by combination[7-10]. Therefore the use of functional initiators is not ideal as the polymer sample may contain a variety of products. Another approach is the use of functional chain transfer agents, discussed in detail in *section 1.4.2*. The use of atom transfer agents such as mercaptans only allows control over the α-end group and typically have the drawbacks of toxicity and colouration[11]. However, chain transfer agents that work by an addition-fragmentation mechanism offer control over functionality of both end groups. For example, Haddleton *et.al.* have shown that dimers produced by catalytic chain transfer polymerisation can be used to produce both α,ω-dihydroxy and dicarboxyl poly(methyl methacrylate)[12,13]. Whilst effective this method is not ideal as molecular weight distributions are ≈ 2 and molecular weight control is limited.

Transition metal mediated living radical polymerisation (TMM-LRP) is an extremely useful method for the production of α-functional polymers due to the facile synthesis of functional halogen initiators. Chain extension reactions of the halogen terminated polymers produced have been researched extensively, however little work has been carried out on modification of the carbon-halogen at the ω-terminus of these polymers. Sawamoto *et al.* have reported the use of silyl enol ethers, *i.e.* α-(trimethylsiloxy)styrene and *p*-methoxy-α-(trimethylsiloxy)styrene, as efficient terminators for polymers prepared by Ru(II)-mediated living polymerisation, discussed further in this chapter[14]. Matyjaszewski *et al.* have described several ways in which the halide end group of polymers prepared by TMM-LRP can be modified. The first is quantitative conversion to an amino end-group via reaction of the C-halide with trimethylsilyl azide to form an azido group which is subsequently reduced with lithium aluminium hydride, *figure 3.1*[15,16]. This has been shown to work for polymers of styrene, MMA and methyl acrylate.

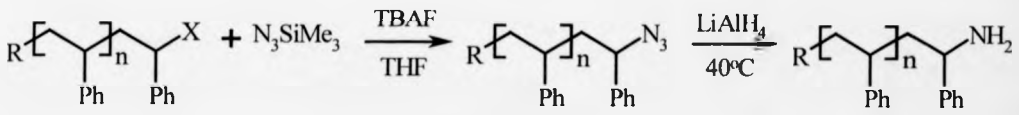


Figure 3.1, Conversion of a carbon halide end group to an amino group

The second reaction is conversion to an alcohol by refluxing with calcium carbonate in a mixture of water and 1,4-dioxane[17]. Their analysis showed that only 70 % of the end groups were converted to the desired hydroxyl end group, with the remaining 30 % being alkene-terminated polystyrene. In the third method used 2-aminoethanol was employed as a nucleophile again producing ω-hydroxyl functional polymer[17]. Using 10 mol equivalents of the amine in presence of triethylamine at room temperature for

48 hours gave 100 % conversion of the C-Br on a polystyrene chain. Matyjaszewski has also reported ω-dehalogenation using tributyltin hydride[18] and the introduction of an allyl group using allyltri-*n*-butylstannane and the use of 1,2-epoxy-5-hexene as non-reactive monomers to introduce the corresponding functionality[19]. Whilst the methods described by Matyjaszewski *et al.* provide methods for producing well-defined telechelics through TMM-LRP the methods require the isolation of the polymer prior to the transformations being carried out. From a commercial perspective this increases the cost of production of such materials and a one pot synthesis is often advantageous.

Recently Coessens *et al.* have shown that addition of allyl alcohol to a polymerisation system causes termination of the reaction. The vinyl bond of the alcohol reacts with the active species produced during the polymerisation and then the chain end is deactivated. Reactivation is not possible due to the absence of stabilising groups near the newly formed carbon-halogen bond, *figure 3.2*[17].

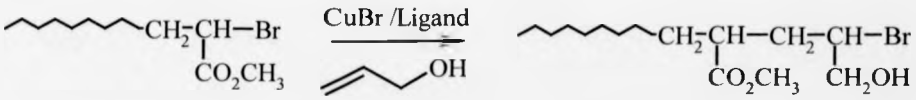


Figure 3.2, TMM-LRP in the presence of allyl alcohol
to produce a ω-hydroxyl functional polymer

This chapter demonstrates several ways in which a specific functional group can be introduced at the ω-terminus of polymethacrylates prepared via copper mediated living radical polymerisation. Transformations described were carried out under similar conditions to the polymerisation reactions. Therefore it is possible to perform these modifications *in situ*, facilitating the chemical process.

The first method involves the homolysis of the ω-C-Br bond with subsequent reaction, via coupling or disproportionation, with an external radical species. For example the reactions carried out using organo tin compounds mentioned above are classified under this approach[18]. Here we examine the use of TEMPO as a scavenger for the carbon-centred radical species formed subsequent to carbon-halogen bond homolysis. In the case of tertiary carbon-centred radicals having an α-methyl group, trapping via disproportionation is competitive with coupling, the latter of which is a reversible process. This ultimately leads to the quantitative formation of a macromonomer and the corresponding hydroxylamine, as described for the reaction of TEMPO with a PMMA chain in *figure 3.3*.

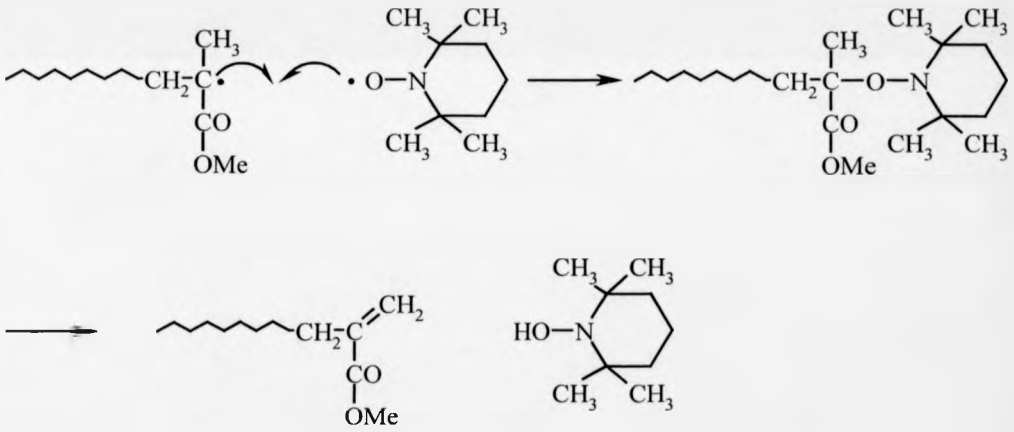


Figure 3.3, Mechanism of irreversible β-hydrogen radical abstraction by TEMPO in the polymerisation of MMA

The second method investigated was the use of vinylic compounds which are unable to undergo homopropagation under free-radical polymerisation conditions, *e.g.* maleic anhydride, *N*-phenylmaleimide, or as reported by Coessens *et al.* for allyl alcohol[17,20]. Under standard TMM-LRP conditions in the presence of one of these monomers a

single unit will be added to the terminus of the polymer and no further propagation can occur.

The third method is closely related to the last, instead of using a monomer that cannot homopropagate a functional monomer that yields a more stable secondary, or primary carbon-halogen bond under TMM-LRP conditions is used. There is a marked difference in the rate of dissociation of the starting *tertiary* C-Br species as compared to the *secondary* or *primary* C-Br due to the relative stabilities of the reactants and the radical centres formed.

The fourth method utilised monomeric species that are able to undergo radical addition, with subsequent fragmentation. Sawamoto *et al.* has previously reported the use of trimethylsilyl enol ethers as quenchers for TMM-LRP to yield polymers with ω-keto functionality and the corresponding trimethylsilyl halide as a by-product, *figure 3.4*[14].

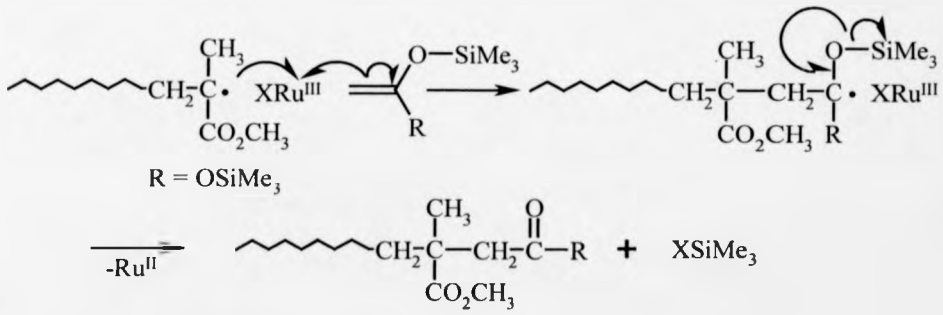


Figure 3.4, Reaction of silyl enol ethers in TMM-LRP

Kharasch *et al.* proposed that allyl bromide undergoes an addition-fragmentation mechanism to explain their results in photochemical studies on addition of trichloromethyl radicals to olefins and in studies on thermal decomposition of diacetyl peroxide in refluxing allyl bromide[21,22]. The proposed mechanism suggested that any

vinyl compound having an α-CH_2Br substituent would undergo an addition-fragmentation reaction and could therefore be used as a chain transfer agent in free radical polymerisation. Meijs[23-27] and Yamada[28,29] have both shown that allyl bromide, methyl α-bromo methacrylate and ethyl α-bromo methacrylate can be used to synthesise α-bromo ω-vinyl functionalised polystyrene and PMMA by chain transfer in conventional free radical polymerisation. The product of the reactions with allyl bromide is an ω-allyl functionalised polymer. It is therefore logical that under TMM-LRP conditions the allyl bromide will undergo the same addition-fragmentation mechanism, *figure 3.5*.

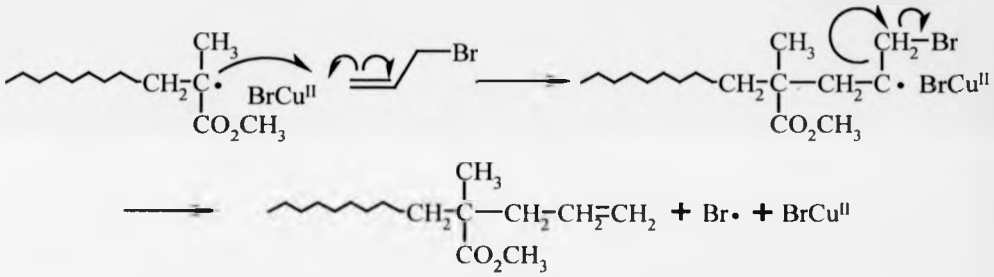


Figure 3.5, Reaction of allyl bromide with ω-bromo PMMA under TMM-LRP conditions

3.1 Results and Discussion

3.1.1 Reaction of ω-bromo PMMA with TEMPO

Tertiary alkoxyamines which have a methyl group α to the alkoxyamine C-O bond undergo competitive irreversible trapping via β-hydrogen radical abstraction versus reversible trapping via coupling after C-O bond homolysis. This accounts for the fact that TEMPO-mediated living radical polymerisation of methacrylates has not yet been proven possible, with proper control of the molecular weight distribution, as a direct result of permanent termination of chain-growth. However, the irreversible process of trapping via disproportionation has advantageous use in the synthesis of macromonomers under TMM-LRP conditions. Addition of TEMPO to a propagating polymerisation solution should terminate the polymerisation process to yield macromonomers, *figure 3.3*.

Methacrylate macromonomers of similar structure have been prepared via CCTP and find commercial applications in pigment dispersants, synthesis of polyols and inks[30]. A characteristic of the polymers produced by this process is that the MWD is relatively broad as a result of the conventional free-radical polymerisation mechanism. Macromonomers prepared via living radical polymerisation, however, would yield products having narrow MWDs. To illustrate this PMMA prepared via TMM-LRP (*Mn* = 3460, PDI = 1.16) was reacted with TEMPO under standard TMM-LRP conditions at 90 °C. The reaction was allowed to proceed for 3 hours. The product was purified by precipitation into pentane. ^{1}H NMR analysis clearly confirmed the presence of the characteristic vinylic protons of these type of macromonomers at 6.16-6.22 ppm and 5.43-5.54 ppm, the ω-methoxy carbonyl

protons at 3.70-3.75 ppm, and the ω-methylene protons at 2.45-2.55 ppm, *figure 3.6*. Comparison of the PMMA starting material with the product using the $CH_3\mathbf{CH_2}O$ protons of the α-initiating group and the resonance of the original ω-methylester as reference shows a high conversion (>78 %) of the ω-bromo PMMA chains into their corresponding macromonomer analogues.

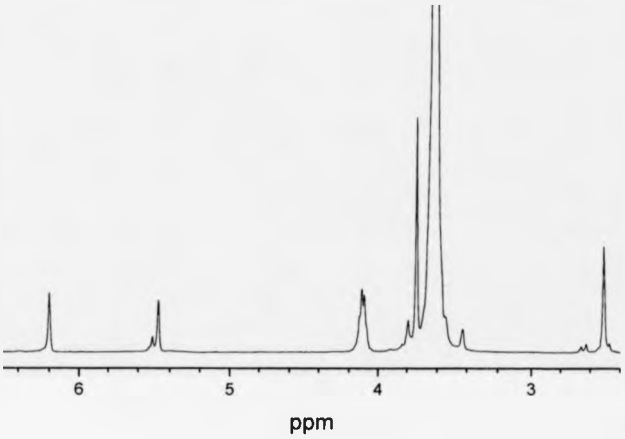


Figure 3.6, Section of the ^{1}H NMR in $CDCl_3$ of the reaction of ω–bromo PMMA with TEMPO to yield macromonomers (see *figure 3.3*), showing the presence of the characteristic vinylic protons at 6.16-6.22 ppm and 5.43-5.54 ppm, the ω-methoxy carbonyl protons at 3.70-3.75 ppm, and the ω-methylene protons at 2.45-2.55 ppm

3.1.2 Reaction of ω-bromo PMMA with Non-Homopropagating Monomers

Maleic anhydride is a common monomer that is not able to homopropagate under free-radical polymerisation conditions, due to an exceptionally low rate coefficient of propagation. Therefore the addition of one monomer unit is carried out easily to give the polymer structure below *figure 3.7*.

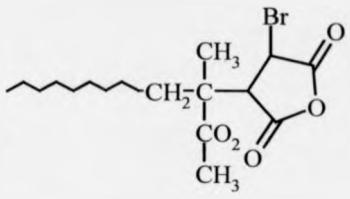


Figure 3.7, Structure of ω-bromo PMMA reacted with maleic anhydride

FTIR analysis confirmed the presence of the targeted endgroup showing the carbonyl stretching of the anhydride at 1781 cm^{-1} adjacent to the C=O stretching of the methoxycarbonyl at 1721 cm^{-1}, *figure 3.8*. Futhermore, ^1H NMR analysis showed complete disappearance of the resonance of the original ω-methylester at 3.75 ppm in d_6-DMSO, thereby indicating a high conversion.

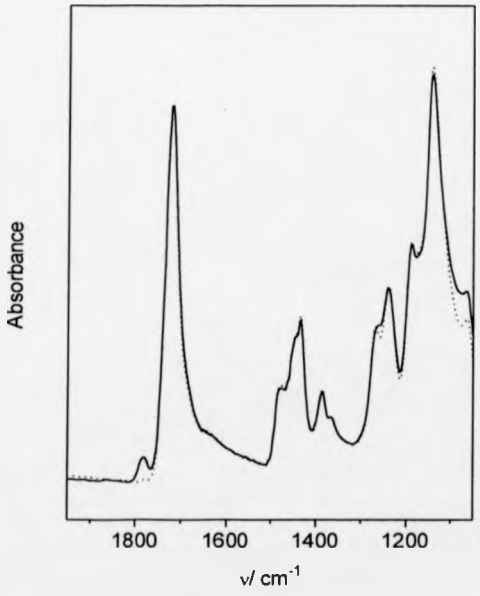


Figure 3.8, Section of the FTIR-spectrum before (·····)and after (——)reaction of ω–bromo PMMA with maleic anhydride (see *figure 3.7*) showing the appearance of the carbonyl stretching of the anhydride at 1781 cm^{-1} adjacent to the C=O stretching of the methoxycarbonyl at 1721 cm^{-1}

3.1.3 Reaction of ω-bromo PMMA with Mono-Substituted Olefins

3.1.3.1 Reaction with Divinylbenzene

Divinylbenzene has a relatively low rate coefficient of homo-propagation and thus guarantees control of polymer chain-growth. In this case the temperature was lowered to ambient conditions, in order to increase the difference in the rate of C-Br homoloysis induced by the difference in activation energies for *secondary* and *tertiary* C-Br species. Reaction at 25 °C for 24 hours resulted in a quantitative addition of one single divinylbenzene monomeric unit onto the PMMA starting material, *figure 3.9.*

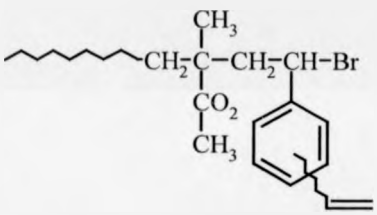


Figure 3.9, Structure of ω-bromo PMMA reacted with divinylbenzene

^{1}H NMR (d_6-DMSO) analysis confirms a quantitative conversion and showed the presence of the aromatic protons at 6.91-7.60 ppm, the three pendant vinyl protons at 6.61-6.86 ppm, 5.68-5.95 ppm and 5.10-5.39ppm, and disappearance of the distinct signal for the ultimate methoxycarbonyl group of the starting material at 3.65-3.80 ppm (see *figure 3.10*). SEC with dual detection provides both DRI (——) and UV (254 nm,) traces, *figure 3.11*. The UV trace extends over the entire range of molecular weight detected by DRI as can be seen by the similarity in the shape of the two traces. The presence of a strong UV chromophore provides supporting evidence for addition of divinylbenzene to the polymer.

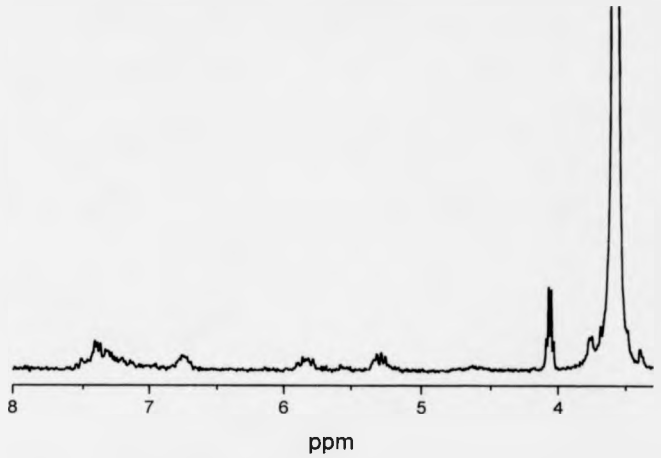


Figure 3.10, Section of the ^{1}H NMR in d_6-DMSO of the reaction of ω–bromo PMMA with divinylbenzene (see *figure 3.9*) showing the aromatic protons at 6.91-7.60 ppm, the three pendant vinyl protons at 6.61-6.86 ppm, 5.68-5.95 ppm and 5.10-5.39 ppm, and disappearance of the distinct signal for the ultimate methoxy carbonyl group of the starting material at 3.65-3.80 ppm

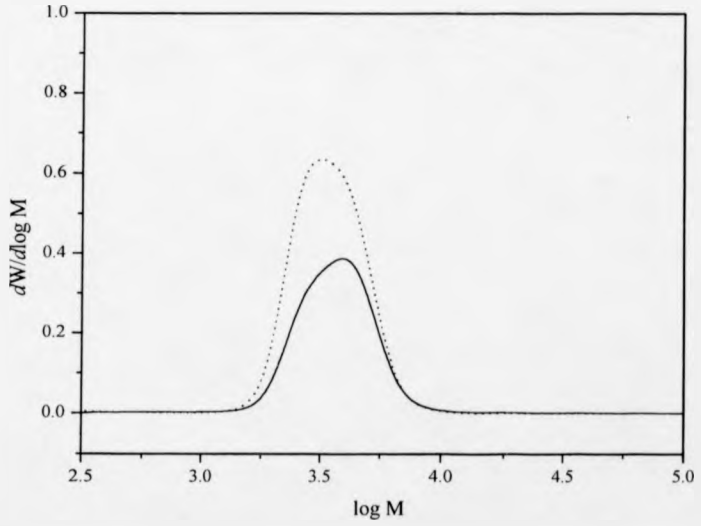


Figure 3.11, (——) Differential Refractive Index SEC chromatogram and (·····) U.V. SEC chromatogram of ω–bromo PMMA reacted with divinylbenzene, *figure 3.8*

3.1.3.2 Reaction with Benzyl Acrylate

Benzyl acrylate has a high rate coefficient of homo-propagation and thus control of chain-growth is more problematic. Comparison of the benzylic resonances, *figure 3.12,* at 5.05-5.18 ppm and the ω-**CH**Br at 4.15-4.36 ppm with the $CH_3\mathbf{CH_2}O$ protons of the α-initiating group at 3.95-4.10 ppm, in the ^{1}H NMR, gave on average *ca.* 3 monomer units added to the starting polymer spectrum under the same polymerisation conditions as with divinylbenzene. In order to circumvent this the initial monomer concentration was reduced by a factor of 10, so as to favour reversible chain-deactivation over monomer addition. This resulted in only 55 % functionalisation. In an attempt to optimise the conditions different amounts of $Cu^{II}Br_2$ were charged into the system to increase the probability of reversible chain-deactivation. It was found that the addition of 22 % $Cu^{II}Br_2$, with respect to $Cu^{I}Br$, with reaction at 60 °C for 4 hours resulted in 62 % transformation, whereas addition of 50 % $Cu^{II}Br_2$ only reached 23 % conversion, as indicated by ^{1}H NMR, *figure 3.13*. Again SEC with UV detection provides supporting evidence for the addition of benzyl acrylate to the polymer, *figure 3.14*.

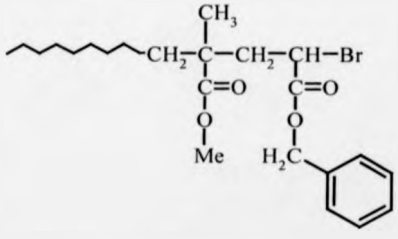


Figure 3.12, Structure of ω-bromo PMMA reacted with benzyl acrylate

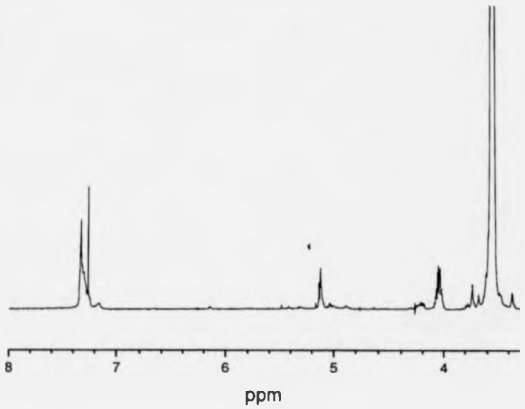


Figure 3.13, Section of the ^{1}H NMR in $CDCl_3$ of the reaction of ω–bromo PMMA with benzyl acrylate, *figure 3.12*

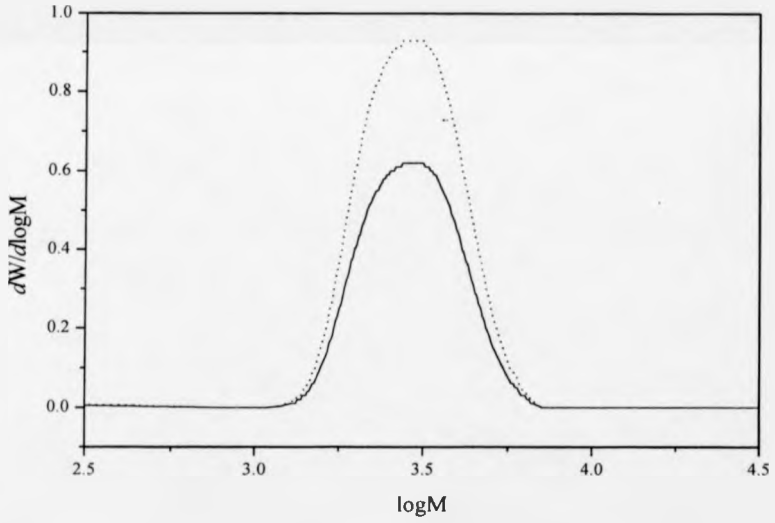


Figure 3.14, (——) Differential Refractive Index SEC chromatogram and (·····) U.V. SEC chromatogram of ω–bromo PMMA reacted with benzyl acrylate, *figure 3.12*

3.1.3.3 Reaction with Ethylene

From a synthetic point of view the reaction of an activated polymer chain with ethylene under TMM-LRP conditions is attractive, as the endgroup will become a primary bromide which is sterically-non hindered. The latter can be transformed into a great variety of different functional groups using well-known organic synthesis reactions, such as nucleophilic substitution reactions. Purging of a TMM-LRP at high conversion (> 85 %) with ethylene, *i.e.* for MMA as a monomer using standard polymerisation conditions for a period of 45 mins, resulted in complete ω-CH_2CH_2Br functionalisation, *figure 3.15*.

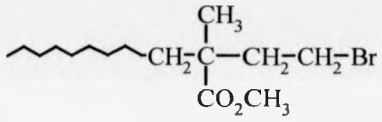


Figure 3.15, Structure of ω-bromo PMMA reacted with ethylene

This was confirmed by both ^1H and ^{13}C NMR analysis, as the resonances of both the ω-OCH_3 (δ 3.65-3.80 ppm) and the C-Br (δ 58-59 ppm) of the starting PMMA disappeared completely and the ^{13}C NMR spectrum showed the presence of the ω-CH_2CH_2Br endgroup, *figure 3.16*.

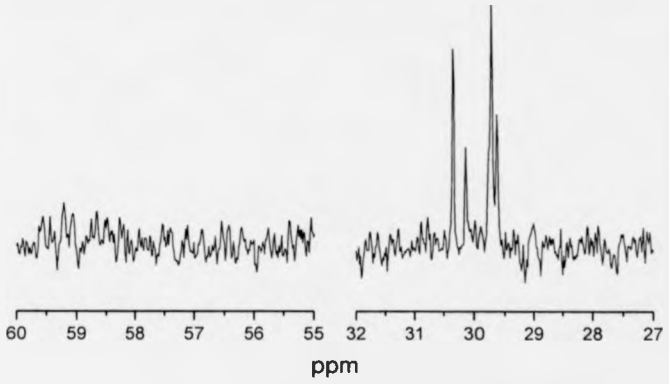
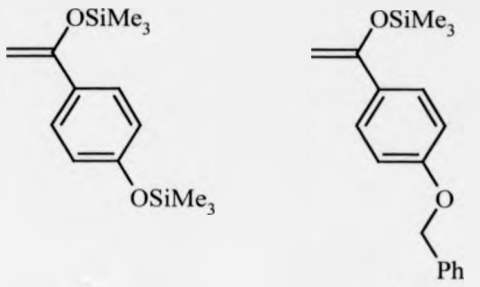


Figure 3.16, Sections of the ^{13}C NMR spectrum in $CDCl_3$ showing the complete disappearance of the quaternary C-Br (δ 58-59 ppm) and the presence of the CH_2CH_2Br resonances after reaction of ω–bromo PMMA with ethylene, *figure 3.15*

3.1.4 Reaction of ω-bromo PMMA with Addition-Fragmentation Agents

3.1.4.1 Reaction with Silyl Enol Ethers

The functional silyl enol ether trimethyl(1-(trimethylsiloxy)-phenylethenyloxy)silane (**A**), *figure 3.17*, was synthesised through reaction of 4'-hydroxyacetophenone with lithium diisopropyl amide at –78 °C and subsequent addition of 2 mole equivalents of chlorotrimethylsilane. Similarly trimethyl(*p*-(benzyloxy)phenylethenyloxy)silane (**B**), *figure 3.17* , was synthesised from 4'-benzyloxyacetophenone.



A **B**

Figure 3.17, **A** Structure of trimethyl(1-(trimethysiloxy)-phenylethenyloxy)silane, **B** Structure of trimethyl(*p*-(benzyloxy)phenylethenyloxy)silane

Following the example of Sawamoto *et al.* the effectiveness of these two silyl enol ethers as quenchers in the transition metal mediated living radical polymerisation of MMA was examined[14]. MMA was polymerised with ethyl-2-bromoisobutyrate initiator and CuBr/N-(*n*-Propyl)-2-pyridylmethanimine complex in toluene at 90 °C for 4 hours. When monomer conversion had reached approximately 50 % (90 mins), the two silyl enol ethers (10 mol equivalents with respect to initiator) were added to the polymerisation reactions. Whilst the control reactions continued to proceed unhindered with the first order rate plot being linear those with added silyl enol ether showed quenching, *figures 3.18 & 3.19*. The final polymer samples were purified by precipitation in pentane and subsequent precipitation in methanol / water (90 : 10). The TMS phenol protecting group was removed by dissolution of the product in a toluene / methanol mixture.

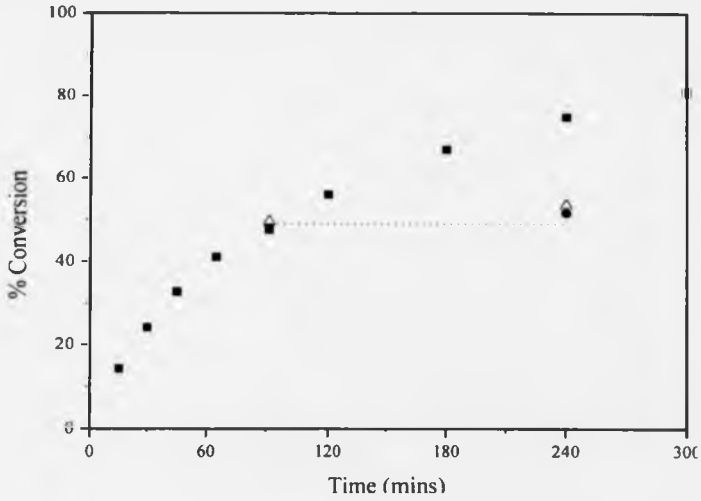


Figure 3.18, Plot of conversion against time for TMM-LRP of MMA in the absence or presence of silyl enol ethers in toluene at 90 °C: [MMA]:[Init]:[Cu]:[Lig] ; 100:2:1:2 Key, ■ Control, △ additon of trimethyl(1-(trimethysiloxy)-phenylethenyloxy)silane and ● addtion of trimethyl(*p*-(benzyloxy)phenylethenyloxy) silane

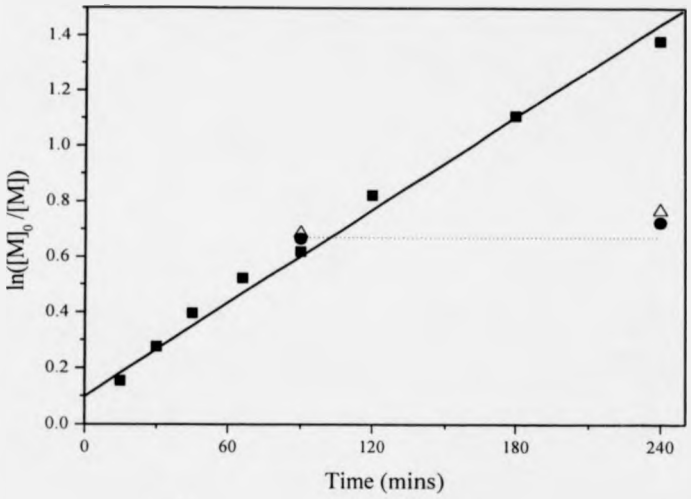


Figure 3.19, Rate plot for TMM-LRP of MMA in the absence or presence of silyl enol ethers in toluene at 90 °C. Key, ■ Control, △ additon of trimethyl(1-(trimethysiloxy)-phenylethenyloxy)silane and ● addtion of trimethyl(*p*-(benzyloxy)phenylethenyloxy)silane

Prior to addition of silyl enol ether at 90 mins all samples were of similar molecular weight with low PDI *ca.* 1.2, *table 3.1*. The PMMA in the control reaction had narrow molecular weight distribution and molecular weight increased proportionally with conversion from 48 % to 75 %. Comparison of the molecular weight data from before and after silyl enol ether addition shows great similarity between *Mn* and PDI and little conversion was observed. However, the fact that any change was observed indicates that although termination by the silyl enol ethers is efficient it is not fast enough to fully eliminate further propagation at the concentration used.

Table 3.1, Molecular weight information for polymerisation of MMA

	90 minutes			240 minutes		
	Control	A	B	Control	A	B
Mn	3800	3200	3100	5000	2800	2800
PDI	1.19	1.19	1.20	1.19	1.36	1.36
% Conv	47.6	48.6	49.6	74.9	51.5	53.6

Dual detection SEC was used to look at the absorption of the quenched sample at 254 nm. The UV traces cover the full range of the DRI traces indicating that throughout the molecular weight distribution the polymer samples are UV active, figures 3.20, 3.21. As the control polymer showed no absorbance at 254 nm it was concluded that the strong UV chromophore is due to the conjugated aromatic ketone present at the ω-terminus of the polymers.

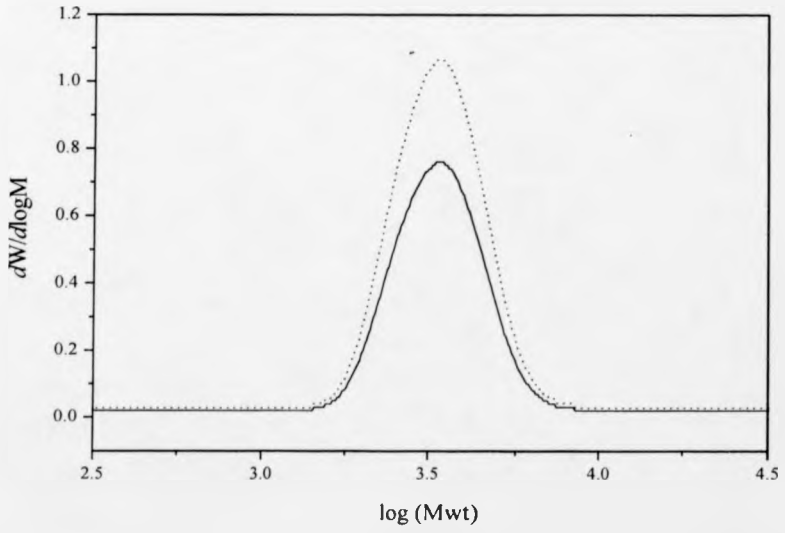


Figure 3.20, (——) Differential Refractive Index SEC chromatogram and (·····) UV SEC chromatogram of PMMA quenched with trimethyl(*p*-(benzyloxy)phenyl ethenyloxy)silane

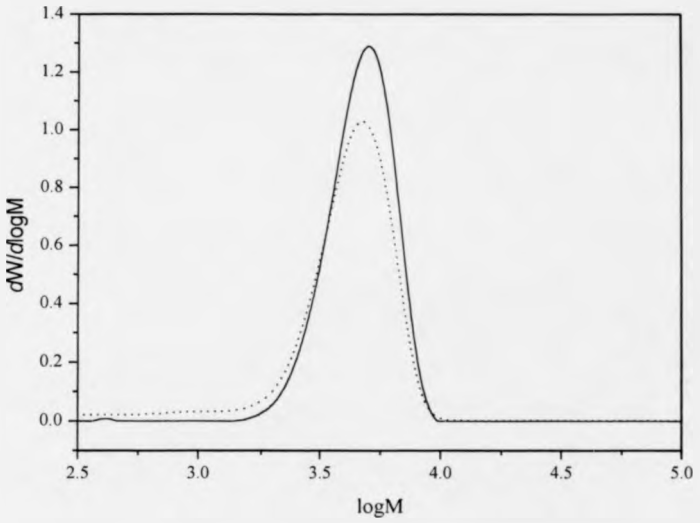
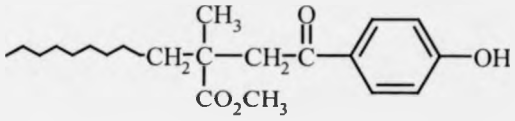


Figure 3.21, (——) Differential Refractive Index SEC chromatogram and (·····) UV SEC chromatogram of PMMA quenched with trimethyl(1-(trimethysiloxy)-phenyl ethenyloxy)silane

Further evidence for the keto terminus was obtained through ^{1}H NMR. *Figure 3.23*, shows the aromatic protons of the ketone end group at 7.68-7.88 ppm and 6.70-6.90 ppm, and the $CH_3\mathbf{CH_2}O$ protons of the α-initiating group at 4.0-4.1 ppm for the polymer sample terminated with trimethyl(1-(trimethysiloxy)-phenylethenyloxy)silane with structure as *figure 3.22* **A**. The absence of the characteristic ω-methoxy carbonyl protons at 3.70-3.75 ppm is also noted. After deprotection of the hydroxyl group by dissolution in toluene / hydrochloric acid solution there is a slight shift in the aromatic protons of the ketone end group to 7.74-7.82 ppm and 6.80-6.89 ppm. Comparison of the relative intensities of the protons of the aromatic group with those of the α-initiating group shows quantitative ω-functionality. Similarly the ^{1}H NMR of the polymer sample terminated by

trimethyl(*p*-(benzyloxy)phenyl ethenyloxy)silane (see *figure 3.22* **B**), clearly shows the aromatic protons of the ketone end group at 7.75-7.95 ppm and 6.92-7.20 ppm, the aromatic protons of the benzyl group at 7.2-7.5 ppm, the O**CH$_2$**Ph and the CH$_3$**CH$_2$**O protons of the α-initiating group at 3.9-4.1 ppm, *figure 3.24*. ω-Functionality was again calculated to be near quantitative and the absence of the ω-methoxy carbonyl protons at 3.70-3.75 ppm should be noted.

A



B

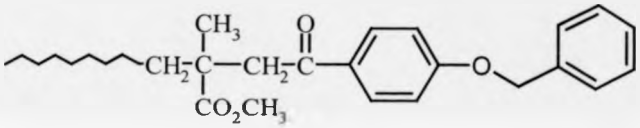


Figure 3.22, **A** Structure of PMMA reacted trimethyl(1-(trimethysiloxy)-phenylethenyloxy)silane and **B** Structure of PMMA reacted with trimethyl(*p*-(benzyloxy)phenylethenyloxy)silane

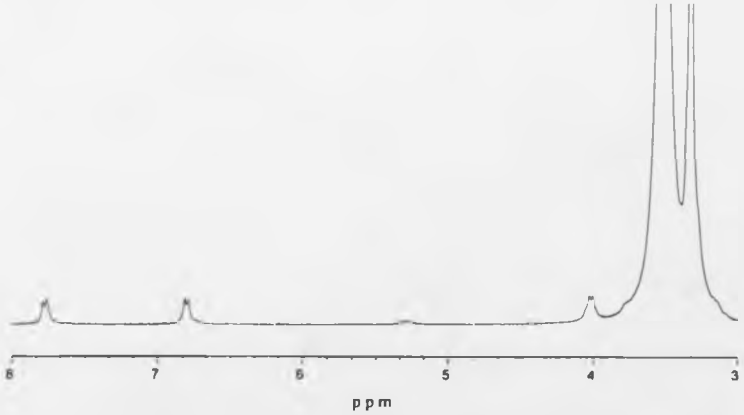


Figure 3.23, Section of the ^{1}H NMR in DMSO of PMMA quenched with trimethyl(*p*-(benzyloxy)phenyl ethenyloxy)silane

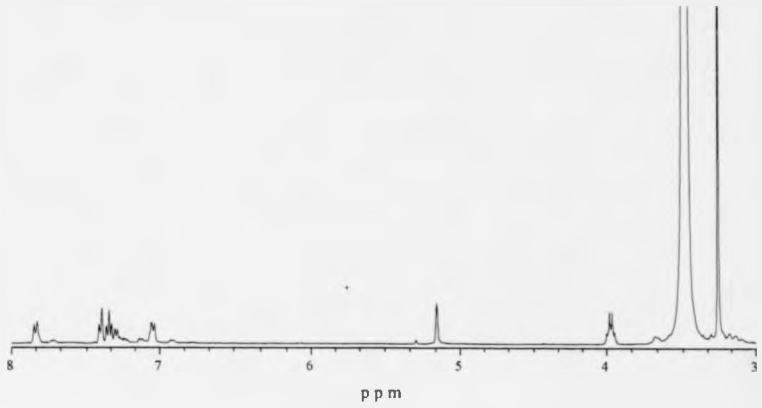


Figure 3.24, ^{1}H NMR in $CDCl_3$ of PMMA quenched with trimethyl(1-(trimethysiloxy)-phenyl ethenyloxy)silane

Alternatively it is possible to functionalise "dormant" PMMA with this type of silyl enol ether. Bromine terminated PMMA and a ten fold excess of trimethyl(1-(trimethysiloxy)-phenylethenyloxy)silane were heated under standard TMM-LRP conditions at 90 °C for 2 hours. The polymer was then purified by passing over activated basic aluminium oxide and precipitation into pentane. Conversion to the ω-ketone was quantitative by ^{1}H NMR analysis.

3.1.4.2 Reaction with Allyl Bromide

It was found that to use allyl bromide as a quenching agent modification of the standard reaction conditions were required. This is due to the elimination of a bromine radical which occurs as a result of the addition-fragmentation. It is possible for the bromine radical to react with the $Cu^{I}Br$ complex to form a $Cu^{II}Br_2$ complex. This increase in Cu^{II} concentration results in an increase in the rate of chain-deactivation

reducing the probability of the addition of allyl bromide consequently inhibiting the modification of the ω-terminus. Through addition of Cu^0, which can disproportionate with Cu^{II} to regenerate Cu^I, it was hoped that this problem would be eliminated[31,32]. The possibility of bimolecular termination by disproportionation was minimised by reducing the temperature to 50 °C thus keeping the rate of generation of carbon-centred radicals low. Under these conditions ^1H NMR analysis showed a functionalisation of *ca.* 57 %, thereby clearly showing the characteristic resonances of the introduced allyl group, *figure 3.25*, at 5.42-5.72 ppm and 4.84-5.06 ppm, *figure 3.26*.

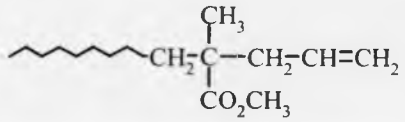


Figure 3.25, Structure of ω-bromo PMMA reacted with allyl bromide

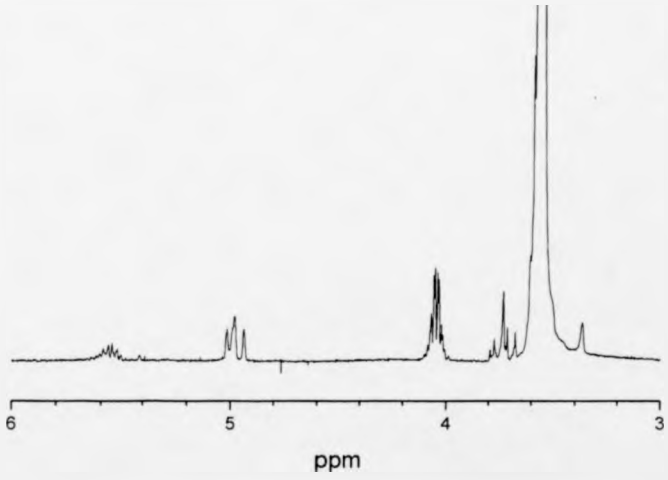


Figure 3.26, Section of the ^1H NMR in $CDCl_3$ of the reaction of ω–bromo PMMA with allyl bromide, *figure 3.25*, showing the characteristic resonances of the introduced allyl group at 5.42-5.72 ppm and 4.84-5.06 ppm

3.2 Conclusion

Modifications of the ω-bromo end group of methacrylate polymers prepared by copper-mediated living polymerisation to produce ω-functional polymers can be performed in high yields using four different approaches, *i.e.*, the use of TEMPO to induce disproportionation, the addition of non-homopropagating monomers, single addition of both fast and slow propagating monomers producing a secondary C-Br bond, and finally the use of compounds which undergo addition-fragmentation.

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Chapter 4

Synthesis of Macromonomers of Tris(trimethylsiloxy)-3-methacryloxy propylsilane

4 Synthesis of Macromonomers of Tris(trimethylsiloxy)-3-methacryloxy propylsilane

A number of methods of preparing vinyl functional oligomers or macromonomers of Tris(trimethylsiloxy)-3-methacryloxy propylsilane (TRIS) have been examined. As discussed in *section 2.2.2* TRIS is a monomer of interest to the contact lens industry due to poly(TRIS) having a high oxygen permeability an essential requirement for contact lens materials. The techniques examined include catalytic chain transfer polymerisation (CCTP) and transition metal mediated living radical polymerisation (TMM-LRP) as well as the use of conventional chain transfer agents.

4.1 Catalytic Chain Transfer Polymerisation of TRIS

4.1.1 Results and Discussion

CCTP is an efficient method for the production of low molecular weight polymers with terminal vinyl functionality, *section 1.5*. *Table 4.1*, summarises the reaction conditions, conversions, molecular weight and polydispersity index of resultant polymers for two independent series of reactions for tris(trimethylsiloxy)-3-methacryloxy propylsilane in 2-butanone at 60 °C, with various concentrations of the catalytic chain transfer agent, CoBF. As the ratio of catalyst to monomer increases a reduction in molecular weight is observed. Unless stated otherwise molecular weights were calculated using *Mark-Houwink* parameters appropriate to PMMA in THF at room temperature. With concentrations of CoBF as low as ~6 ppm resultant polymer has an *Mn* of just 5000 $g.mol^{-1}$. This is a very significant decrease from the *Mn* values

of 477000 and 240000 obtained when no chain transfer agent is present in the system. Though the cobalt catalyst is highly coloured, at the low concentrations of 6 ppm resultant polymer is found to be clear with no purification required to remove the catalyst. It is observed that as the ratio of CoBF to monomer is increased there is a decrease in conversion and narrowing of the polydispersity index of the resultant polymer.

Table 4.1, Reaction Conditions and Molecular Weight/Conversion Data for Polymerisation of Tris(trimethylsiloxy)-3-methacryloxy propylsilane in 2-Butanone at 60 °C in the Presence of CoBF

	2-Butanone (% w/w)	AIBN (% w/w)	[CoBF]/ [TRIS]×10^6	*Mn*	*Mw*	PDI	% Conv
A1	41	0.14	0	477000	845000	1.77	11.4
A2	41	0.14	3.17	10700	33800	3.15	11.2
A3	41	0.14	6.34	4920	11100	2.26	10.3
A4	41	0.14	12.7	3180	6170	1.94	8.6
A5	41	0.14	25.3	2060	2660	1.29	5.4
B1	41	0.20	0	240000	459000	1.91	13.6
B2	41	0.20	2.99	19000	33900	1.78	12.6
B3	41	0.20	5.98	4980	6940	1.39	13.0
B4	41	0.20	12.0	3060	3940	1.29	10.6
B5	41	0.20	23.9	2350	3080	1.30	6.1

The effectiveness of a chain transfer agent is given as the chain transfer constant, *Cs*, *section 1.4.2.1*. Knowledge of the value of *Cs* allows prediction of the quantity of catalyst required to produce polymer of a desired molecular weight. *Table 4.2*, contains the chain transfer constant data for the two independent sets of

polymerisations and associated *Cs* values calculated using the four methods previously described.

Table 4.2, Chain Transfer Constant Data for Polymerisation of Tris(trimethylsiloxy)-3-methacryloxy propylsilane in 2-Butanone at 60 °C in the Presence of CoBF

	DP_n	$1/DP_n$ ($\times10^3$)	DP_w	$2/DP_w$ ($\times10^3$)	*1/DP$_n$ plot*	*1/DP$_n$ equation*	*2/DP$_w$ plot*	*2/DP$_w$ equation*
A1	1128	8.87	1999	1.00	-	-	-	-
A2	25.34	39.46	79.92	25.02	-	12200	-	7580
A3	11.63	85.95	26.32	76.00	-	13400	-	11800
A4	7.51	133.13	14.60	136.99	-	10400	-	10700
A5	4.86	205.55	6.30	317.67	-	8070	-	12500
				Cs	7840 ± 920	11030 ± 2320	12620 ± 570	10660 ± 2180
B1	567	1.77	1085	1.84	-	-	-	-
B2	45.03	22.21	80.15	24.95	-	6840	-	7730
B3	11.79	84.80	16.41	121.85	-	13900	-	20100
B4	7.24	138.18	9.32	214.63	-	11400	-	17800
B5	5.57	179.39	7.27	274.92	-	7430	-	11400
				Cs	7530 ± 1470	9890 ± 3350	11810 ± 2330	14260 ± 5690

It should be noted that PMMA standards were used for the SEC calibration and the samples analysed using *Mark-Houwink* parameters, K and α, appropriate to PMMA in THF at room temperature, thus molecular weights are not absolute and merely relative to PMMA ($K = 10.4\times10^{-5}$ dl g^{-1} and $\alpha = 0.697$), *equation 4.1*.

$$[\eta] = KM^{\alpha} \qquad \textbf{(4.1)}$$

Providing K and α values are known for a polymer sample that differs to that of the calibrant the calibration curve allows universal calibration as the following holds, *equation 4.2*.

$$[\eta]_1 \times M_1 = [\eta]_2 \times M_2 \qquad \textbf{(4.2)}$$

Where 1 and 2 refer to the calibrant and analyte respectively. Substituting *equation 4.1* into *equation 4.2* and subsequent rearrangement yields *equation 4.3*.

$$M_2 = \left(\frac{K_1}{K_2}\right)^{\frac{1}{1+\alpha_2}} \times M_1^{\frac{1+\alpha_1}{1+\alpha_2}} \qquad \textbf{(4.3)}$$

Muratore *et al.* have determined the *Mark-Houwink* constants for TRIS in THF at room temperature to be $K = 1.67\times10^{-5}$ dl g^{-1} and $\alpha = 0.74$[1]. Therefore it has been possible to calculate true values of *Mn* and *Mw* for the polymerisations and thus recalculate the *Cs* values for this system, see *tables 4.3 & 4.4*.

Table 4.3, Number Average Molecular Weight and Chain Transfer Constant Data for Polymerisation of Tris(trimethylsiloxy)-3-methacryloxy propylsilane (TRIS) in 2-Butanone at 60 °C in the Presence of CoBF using TRIS *K* and α Values.

	Mn	DP_n	$1/DP_n \times 10^3$	*1/DP$_n$ plot*	*1/DP$_n$ eqn.*
A1	988000	2335.50	0.43	-	-
A2	24400	57.64	17.35	-	5340
A3	11400	26.98	37.07	-	5780
A4	7440	17.61	56.80	-	4450
A5	4870	11.53	86.76	-	3410
			Cs	3300 ± 400	4740 ± 1050
B1	505000	1193.53	0.84	-	-
B2	42700	100.98	9.90	-	3030
B3	11600	27.34	36.58	-	5980
B4	7180	16.98	58.89	-	4860
B5	5570	13.16	75.97	-	3140
			Cs	3180 ± 630	4250 ± 1420

Table 4.4, Weight Average Molecular Weight and Chain Transfer Constant Data for Polymerisation of Tris(trimethylsiloxy)-3-methacryloxy propylsilane (TRIS) in 2-Butanone at 60 °C in the Presence of CoBF using TRIS *K* and α Values.

	Mw	DP_w	$2/DP_w \times 10^3$	*2/DP$_w$ plot*	*2/DP$_w$ eqn.*
A1	1730000	4082.54	0.49	-	-
A2	74700	176.71	11.32	-	3420
A3	25300	59.80	33.44	-	5200
A4	14200	33.66	59.41	-	4650
A5	6270	14.82	134.93	-	5300
			Cs	5340 ± 220	4640 ± 870
B1	951000	2248.04	0.89	-	-
B2	74900	177.19	11.29	-	3480
B3	16000	37.74	53.00	-	8720
B4	9190	21.73	92.05	-	7630
B5	7220	17.07	117.19	-	4860
			Cs	5020 ±1000	6170 ± 2420

Figures 4.1 & 4.2, show plots of $1/DP_n$ and $2/DP_w$ respectively vs. [CoBF]/[TRIS]. The solid lines are those of series A and the broken lines those for series B, the two sets of data for each series arise from using K and α values for PMMA or TRIS.

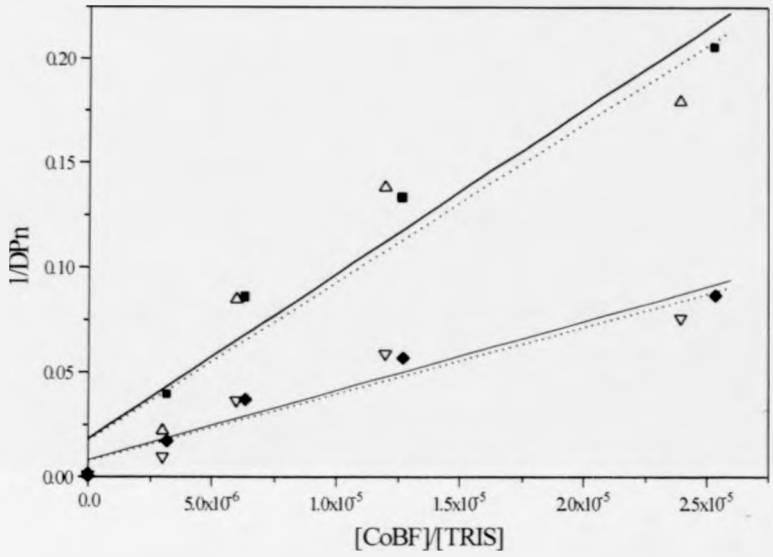

Figure 4.1, *Mayo-plot* for the Polymerisation of Tris(trimethylsiloxy)-3-methacryloxy propylsilane in 2-Butanone at 60 °C in the Presence of CoBF. Data Set A, ■ PMMA K and α values, ◆ TRIS K and α values, (——) line of best fit, Cs = 7840 and 3300 respectively. Data Set B, △ PMMA K and α values, ▽ TRIS K and α values, ( ) line of best fit, Cs = 7530 and 3180 respectively.

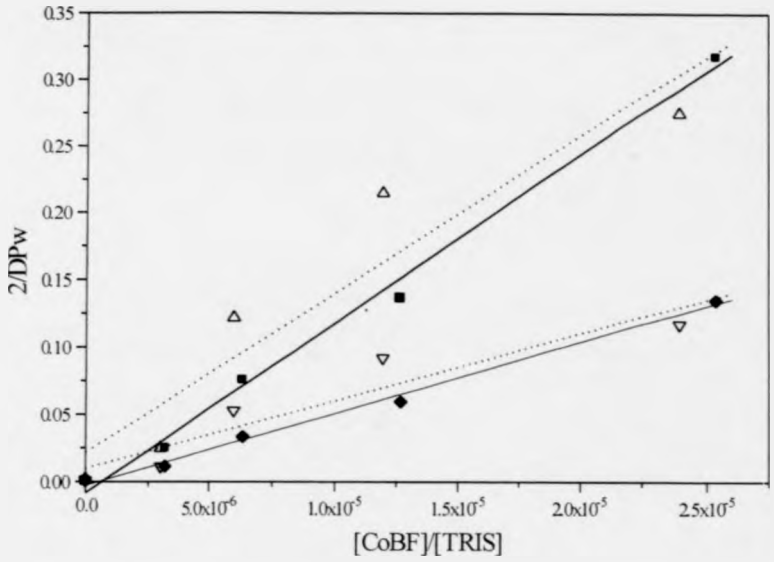

Figure 4.2, *Mayo-plot* for the Polymerisation of Tris(trimethylsiloxy)-3-methacryloxy propylsilane in 2-Butanone at 60 °C in the Presence of CoBF. Data Set A. ■ PMMA K and α values. ◆ TRIS K and α values. (——) line of best fit, Cs = 12620 and 5340 respectively. Data Set B. △ PMMA K and α values. ▽ TRIS K and α values. ( ) line of best fit, Cs = 11810 and 5020 respectively.

The Cs values obtained for both sets of reactions are consistent; *i.e.* the *Mayo-plots* for both series A and B (PMMA K and α values) give values within experimental error. However, there are inconstancies between the different methods of analysis. It is interesting to note the difference between the Cs values calculated from molecular weights obtained with either PMMA or TRIS K and α values and shows the importance of correct molecular weight information. The Cs values calculated through simple substitution have substantial associated errors, highlighting the insufficient method of averaging used to obtain these values. The values of 3300 and 3180 obtained from $1/DP_n$ plots are substantially lower than the values of 5340 and 5020

obtained from $2/DP_w$ plots (using *Mark-Houwink* constants for TRIS) this demonstrates the significance of error in *Mn* values obtained by SEC in the low molecular weight region. It is also noted that molecular weights obtained by SEC using *Mark-Houwink* constants appropriate to PMMA are consistent with molecular weights obtained by ^{1}H NMR analysis for low molecular weight samples. When *Mark-Houwink* constants for TRIS are used the values are considerably higher than those obtained by ^{1}H NMR analysis.

From closer inspection of the *Mayo-plots*, *figures 4.1 & 4.2*, it can be seen that the slopes are generally non-linear. From *table 4.1* we observe that as the catalyst concentration increases, conversion and polydispersity decrease. As conversion increases the ratio of catalyst to monomer increases resulting in a greater reduction in molecular weight and a broadening in the molecular weight distribution. The decrease in conversion with increase in catalyst concentration suggests a decrease in rate of polymerisation and may be explained by non-efficient reinitiation of monomer by Co(III). TRIS has a high affinity for oxygen and it is possible that routine deoxygenating techniques are not sufficient, therefore the presence of oxygen should be considered. The presence of oxygen in the system could easily oxidise the CoBF which would cause a reduction in the observed Cs[2]. It is known that propagating radicals can reduce this Co(III) derivative back to the active Co(II) complex[3]. If this were to occur then the concentration of active catalyst would increase with conversion causing a decrease in molecular weight and an increase in polydispersity index. For a fixed level of oxygen the fraction of poisoned catalyst would be more significant for polymerisations with low levels of CoBF and therefore the observed results would be expected.

Muratore *et al.* have recently calculated the *Cs* of TRIS in toluene (67 % v/v) at 60 °C to be approximately 1400 based on *Mw* values obtained through SEC with *K* and α values appropriate to TRIS. This is significantly lower than the value of approximately 5300 obtained through current calculations. Muratore *et al.* put forward reasons for such low *Cs* values that also help to explain the poor molecular weight control they observed. The most interesting of which is their belief that due to the high oxygen affinity of TRIS, standard deoxygenation through purging with nitrogen is insufficient. This would result in varying levels of oxygen in different sample preparations leading to greater error in *Cs* calculations. Indeed preliminary reactions carried out in bulk and deoxygenated via nitrogen purging agree with the findings of Muratore *et al.* showing little control and molecular weights did not correlate to the concentration of catalyst present, *table 4.5*.

Table 4.5, Polymerisation of Tris(trimethylsiloxy)-3-methacryloxy propylsilane in Bulk at 60 °C in the Presence of CoBF Deoxygenation by Nitrogen Purging

	wt % AIBN	[CoBF]/ [TRIS]×10^6	*Mn* (SEC)	*Mw* (SEC)	PDI	*Mn* (NMR)	% Conv
D1	0.2	2.9	2420	3600	1.49	2420	98
D2	0.2	5.7	1660	2040	1.23	1770	92
D3	0.2	19.0	3240	5540	1.71	3120	95
D4	0.2	25.8	1740	2170	1.25	-	47
D5	0.2	32.0	2860	4900	1.71	2420	82

Reactions carried out in 2-butanone (41 % w/w) deoxygenated using more stringent methods, *i.e.* both monomer and reaction solutions deoxygenated via four consecutive freeze, pump, thaw cycles, showed more continuity and molecular weights correlate well with those predicted from the calculated *Cs*, *table 4.6*.

Table 4.6, Polymerisation of Tris(trimethylsiloxy)-3-methacryloxy propylsilane in 2-Butanone at 60 °C in the Presence of CoBF Deoxygenated by four Freeze, Pump Thaw Cycles

	wt % AIBN	[CoBF]/ [TRIS] $\times 10^6$	*Mn* (SEC)	*Mw* (SEC)	*Mn* (NMR)	PDI	% Conv
E1	0.2	20.2	3410	5390	3480	1.55	100
E2	0.2	5.6	6120	9870	6990	1.61	96
E3	0.15	6.2	5400	10500	5720	1.95	94
E4	0.15	12.4	2600	5530	2870	2.10	92

The ^{1}H NMR spectra of these polymers clearly shows the characteristic resonances of the vinyl protons indicative of macromonomers produced through CCTP, confirming the activity of the CoBF, *figure 4.3*.

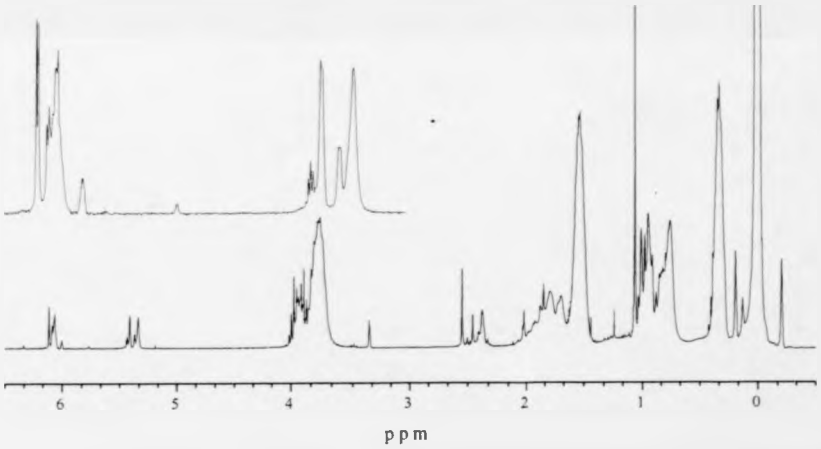

Figure 4.3, ^{1}H NMR in $CDCl_3$ of poly(tris(trimethylsiloxy)-3-methacryloxy propylsilane macromonomer (*Mn* 3240) prepared in the presence of CoBF. Macromonomer vinyl proton resonances at 6.08-6.15 ppm and 5.28-5.46 ppm are shown in the insert

Examination of the rate of polymerisation for one of these polymerisations, *figure 4.4*, shows 50 % conversion after just 4 hours. Replotting the data as a kinetic plot shows no induction period with conversion increasing linearly with time. Evolution of

molecular weight with conversion is given in *table 4.7* for this polymerisation. *Mn* slowly increases with conversion with molecular weight distribution gradually broadening, although there is no noticeable change in the shape of the mass envelope.

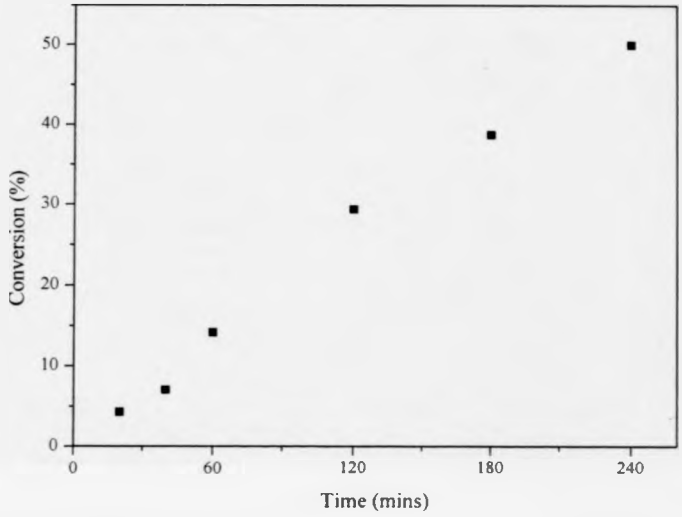

Figure 4.4, Conversion vs. time for catalytic chain transfer polymerisation of TRIS

Table 4.7, Molecular Weight and Conversion Data for the CCTP of TRIS

Time	Conversion (%)	*Mn*	*Mw*	PDI
20	4.3	4180	5870	1.40
40	7.0	4840	7260	1.50
60	14.2	5460	8170	1.50
120	29.4	4650	8390	1.80
180	38.8	5400	10550	1.95
240	50.0	5510	10550	1.92

Previous studies at Warwick University have shown that addition of solvent can cause great reductions in the effectiveness of the cobalt catalysts used in CCTP. Typically *Cs* values for MMA in bulk at 60 °C using CoBF as the CCTA are approximately

40000[4]. When co-ordinating solvents such as methanol and 2-butanone are introduced to this system (66 % v/v) a dramatic reduction in *Cs* is observed with reported values of between 10000 and 26000 respectively[4]. These values are for distilled solvents and in the case of 2-butanone if not distilled a *Cs* as low as 8000 was observed[4]. This has been explained due to the presence of trace acidic impurities which may lead to hydrolysis of the catalyst. It is interesting to note that the reductions in *Cs* are not due to dilution effects as when methyl isobutyrate, the saturated analogue of MMA, is employed as a solvent there is no reduction in *Cs* from that of the value reported for bulk polymerisation[5]. Haddleton *et al.* have explained these observations as a result of competition between monomer, polymer and co-ordinating solvent at the Co-centre[4]. This is consistent with the fact that methanol is a stronger co-ordinating solvent than 2-butanone. However, toluene is only weakly co-ordinating and yet a *Cs* of only 20000 (for distilled toluene) is observed, the reason for this effect remains unexplained[6]. The variation in type of solvent and concentration could explain the disparity between our results and those of Muratore *et al.* Even considering solvent effects a $Cs \approx 5000$ is lower than would be expected. The propagation rate coefficient of TRIS has been calculated by pulsed laser polymerisation and found to be only ~30 % higher than that of MMA and therefore does not fully account for the low value[1,7]. The chain transfer reaction is fast and therefore believed to be diffusion controlled, so the higher viscosity of TRIS would lead to a lower chain transfer rate coefficient and hence a lower *Cs*[1,4,8]. The extent to which viscosity effects the system is limited and does not account for such a significant reduction.

4.1.2 Conclusion

It has been shown that macromonomers of TRIS can be produced by catalytic chain transfer polymerisation. However, molecular weight control is relatively difficult due to reproducibility problems which are presumed to be due to oxygen poisoning of the Co(II) catalyst. This can be overcome if more stringent reaction conditions are employed and every effort is taken to remove oxygen from the system.

4.1.3 Copolymerisation of TRIS with HEMA

An alternative approach to the production of TRIS macromonomers is by copolymerisation of TRIS with a hydroxyl functional monomer *e.g.* hydroxyethyl methacrylate (HEMA) and subsequent transformation of the hydroxyl groups with isocyanatoethyl methacrylate. Each macromolecule within the polymer distribution will have varying degrees of functionality and there is no certainty that all chains will contain at least one of the unsaturated groups.

4.1.3.1 Results and Discussion

Molecular weight of this polymer was controlled by the addition of a small quantity, 20 ppm, of CoBF. CoBF, AIBN (0.23 wt %), TRIS and 20 mol % of HEMA were placed in a Schlenk and deoxygenated by four consecutive freeze, pump, thaw cycles. The polymerisation was carried out under an inert atmosphere of nitrogen at 60 °C for 48 hours. The *Mn* of the polymer was found to be 963 with a PDI = 1.38 by SEC. ^{1}H NMR analysis clearly confirms the presence of characteristic vinyl protons from

CCTP at 6.10-6.26 ppm and 5.40-5.59 ppm, *figure 4.5* **A**. Full assignment of the spectrum allows polymer composition and *Mn* to be calculated. For TRIS the following protons are assigned, $O\mathbf{CH_2}$ 3.67-4.32 ppm, $OCH_2\mathbf{CH_2}$ 1.48-1.77 ppm and $\mathbf{CH_2}Si$ 0.32-0.54 ppm. The $O\mathbf{CH_2}$ and $\mathbf{CH_2}OH$ of HEMA are obscured by the $O\mathbf{CH_2}$ of the TRIS at 3.67-4.32 ppm. The polymer was found to contain 24.6 % HEMA, an average of 0.86 per chain withthe *Mn* calculated at 1230.

Hydroxyl groups present in the oligomer were reacted with isocyanatoethyl methacrylate. The polymer was dissolved in chloroform and 1.1 mole equivalents of isocyanatoethyl methacrylate and 0.13 mole equivalents of dibutyltin dilaurate as catalyst. A small quantity of 2,6-Di-*tert*-butyl-4-methylphenol was added as radical inhibitor. The solution was refluxed for 5 hours and subsequently methanol was added so as to destroy the excess/unreacted isocyanate and the solution was allowed to stand at ambient temperature overnight. The solution was washed three times with deionised water and the organic layer was dried over magnesium sulphate. Following filtration the macromonomer was isolated in vacuo.

SEC analysis showed the *Mn* of the oligomer to be 1750, PDI = 1.24. ^{1}H NMR of the purified polymer confirmed quantitative conversion of the hydroxyl groups through analysis of the $NHCH_2\mathbf{CH_2}CO_2$ protons of the vinyl containing units at 3.18-3.52 ppm and the $OCH_2\mathbf{CH_2}$ protons on TRIS at 1.42-1.70 ppm. The resonance of the vinylic protons at 5.89-6.23 ppm and 5.32-5.62 ppm is also visible, see *figure 4.5*, **B**.

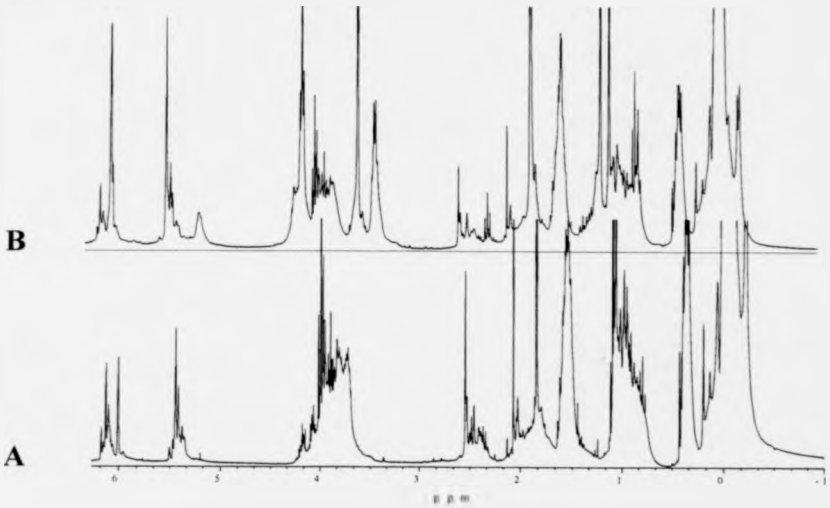

Figure 4.5, ^{1}H NMR in $CDCl_3$ of **A** TRIS/HEMA copolymer, vinylic protons at 6.10-6.26 ppm and 5.40-5.59 ppm, O**CH$_2$** and HEMA O**CH$_2$CH$_2$**OH at 3.67-4.32 ppm, OCH$_2$**CH$_2$** at 1.48-1.77 ppm and **CH$_2$**Si at 0.32-0.54 ppm and **B** after reaction with isocyanatoethyl methacrylate the presence of the vinylic protons at 5.89-6.23 ppm and 5.32-5.62 ppm, and the appearance of the following resonances: α-CO$_2$**CH$_2$CH$_2$**CO$_2$NH at 3.68-4.30ppm, α-**NH** at 5.00-5.25 ppm, α-NH**CH$_2$** at 3.45-3.68 ppm, α-NHCH$_2$**CH$_2$**CO$_2$ at 3.18-3.52 ppm and the OCH$_2$**CH$_2$** protons of TRIS at 1.42-1.70

4.1.3.2 Conclusion

This method of macromonomer production is effective for producing a polymer that has an approximate 100 % vinyl functionality. Higher molecular weight samples would contain more HEMA groups and therefore after coupling with glycidyl methacrylate would contain a higher proportion of vinyl functionality.

4.2 Use of Functional Mercaptan Chain Transfer Agents

In 1995 McGee and Valint reported the production of TRIS macromonomers in a patent covering the production of hydrophilic silicone contact lenses[9]. They reported the use of mercaptoacetic acid and mercaptoethanol as chain transfer agents to produce α-monofunctional TRIS oligomers. Radicals (R') present in the system are capable of abstracting a hydrogen from the mercaptan. In the case of a propagating chain this will cause premature termination and thus a reduction in the observed molecular weight of polymers produced. The newly formed radical of the mercaptan can initiate a new chain which may then undergo propagation, this sequence of events is outlined by *figure 4.6* for mercaptoacetic acid.

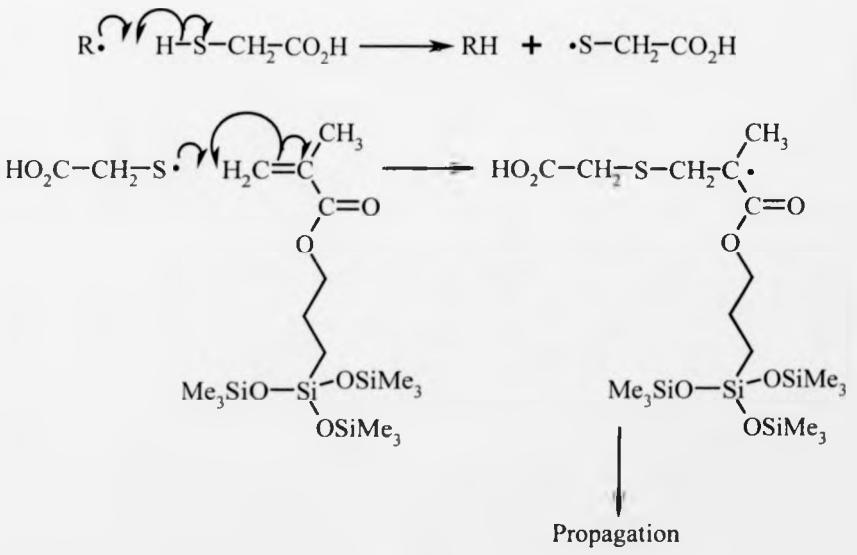

Figure 4.6, Chain Transfer Reaction of Mercaptoacetic acid with TRIS

The limitations of this method of producing end functional materials are the same as for CCTP *i.e.* initiation and termination do not occur solely through reactions involving mercaptan chain transfer. The initiator used for this polymerisation accounts for a small percentage of the α terminus of the polymer material. To increase the percentage functionality an initiator which yields an analogous end group to that of the chain transfer agent should be used. Termination by disproportionation and combination occurs to some extent with termination by combination resulting in difunctional polymers. The relative amount of termination through disproportionation and combination can be minimised by maintaining a low radical flux and rate of polymerisation.

Once the oligomers were prepared McGee and Valint transformed the end groups to give vinyl functionality. In the case of the oligomer prepared with mercaptoacetic acid the acetic acid end group was reacted with glycidyl methacrylate. Similarly, the hydroxyl end group of the oligomer prepared with mercaptoethanol was reacted with 2-isocyanatoethyl methacrylate, *figure 4.7*.

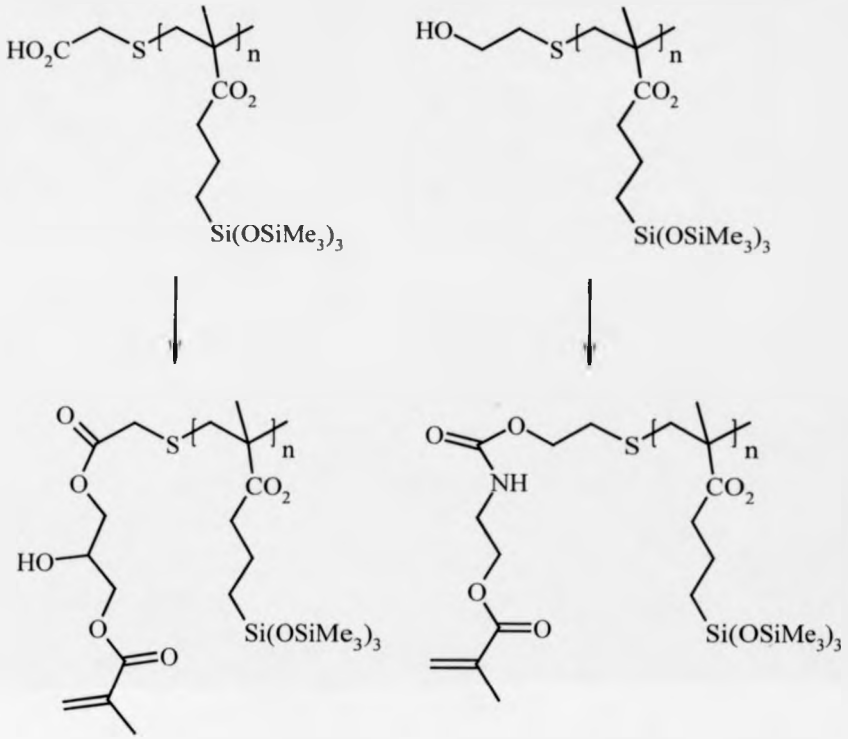

Figure 4.7, TRIS Macromonomers from conversion of α-terminus carboxylic acid and hydroxyl residues

4.2.1 Results and Discussion

4.2.1.1 Polymer Synthesis

The procedures of McGee and Valint were repeated to produce two oligomeric macromonomers of TRIS. TRIS was polymerised in bulk with AIBN (0.5 % w/w) in the presence of either mercaptoacetic acid or mercaptoethanol (26.5 mol %), the mixture was deoxygenated by purging with nitrogen prior to heating to 60 °C for 72 hours. ^{1}H NMR analysis at this time showed that 100 % conversion had been reached. The polymers were purified by dissolving in diethyl ether and washing three times with deionised water. The organic layer was dried over magnesium sulphate and

following filtration the polymer was isolated in vacuo. The polymer with carboxylic acid end group had an *Mn* of 1900, *Mw* 2300 and PDI 1.23. ^{1}H NMR analysis of the purified polymer confirmed the incorporation of the mercaptan by the presence of the α-S**CH$_2$**CO$_2$H resonance at 3.10-3.30 ppm, *figure 4.8* **A**. The hydroxyl functional polymer had an *Mn* of 1900, *Mw* 2300 and PDI 1.19 by SEC. Again ^{1}H NMR analysis confirmed the presence of the hydroxyl terminus, **CH$_2$**OH resonance at 3.55-3.75 ppm and α-S**CH$_2$** resonance at 2.52-2.75 ppm, *figure 4.9***A**. Integration of the O**CH$_2$** (3.75-4.12 ppm) and **CH$_2$**Si (0.32-0.58 ppm) resonances of TRIS and **CH$_2$**OH (3.55-3.75 ppm) resonance of the end group gave an *Mn* of 1600 g.mol^{-1}. The polydispersity of both oligomers were much lower than expected for chain transfer radical polymerisation due to the low degree of polymerisation of the oligomers produced.

4.2.1.2 Coupling of Carboxylic Acid Functional Polymer with Glycidyl Methacrylate

The carboxylic acid functionalised intermediate polymer was converted to macromonomer through reaction of the acid group with glycidyl methacrylate in toluene with N,N-dimethyldodecylamine as catalyst. ^{1}H NMR analysis confirmed the presence of the characteristic vinyl protons at 5.51-5.61 ppm and 6.02-6.16 ppm, *figure 4.8* **B**. Integration of the vinylic proton resonance and the **CH$_2$**Si of TRIS at 0.32-0.62 ppm gave *Mn* 1600 which correlates well with the value obtained from SEC.

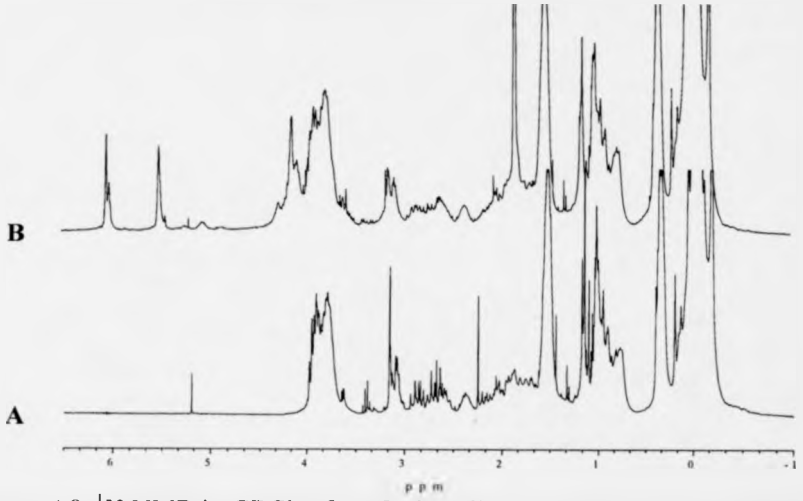

Figure 4.8, ^{1}H NMR in $CDCl_3$ of **A)** Carboxylic acid functional poly(TRIS) showing the OCH_2 (3.7-4.1 ppm), α-SCH_2CO_2H (3.10-3.30 ppm) and CH_2Si (0.32-0.58 ppm) resonances and **B)** after reaction with glycidyl methacrylate the presence of the vinylic protons at 5.51-5.61 ppm and 6.02-6.16 ppm

4.2.1.3 Coupling of Hydroxyl Functional Polymer with Isocyanatoethyl Methacrylate

The hydroxyl functional intermediate polymer was coupled with isocyanatoethyl methacrylate to give the polymer an unsaturated polymerisable functional group, *section 4.1.3*. ^{1}H NMR analysis confirmed the presence of the characteristic vinyl protons at 5.55-5.60 ppm and 6.07-6.13 ppm, see *figure 4.9* **B**. Integration of the vinylic proton resonance and those of the CH_2Si of TRIS at 0.32-0.54 ppm the *Mn* of the polymer was calculated to be 1900g.mol^{-1}. A comparison of the ^{1}H NMR spectra showed quantitative conversion of the hydroxyl by disappearance of the α-CH_2OH resonance.

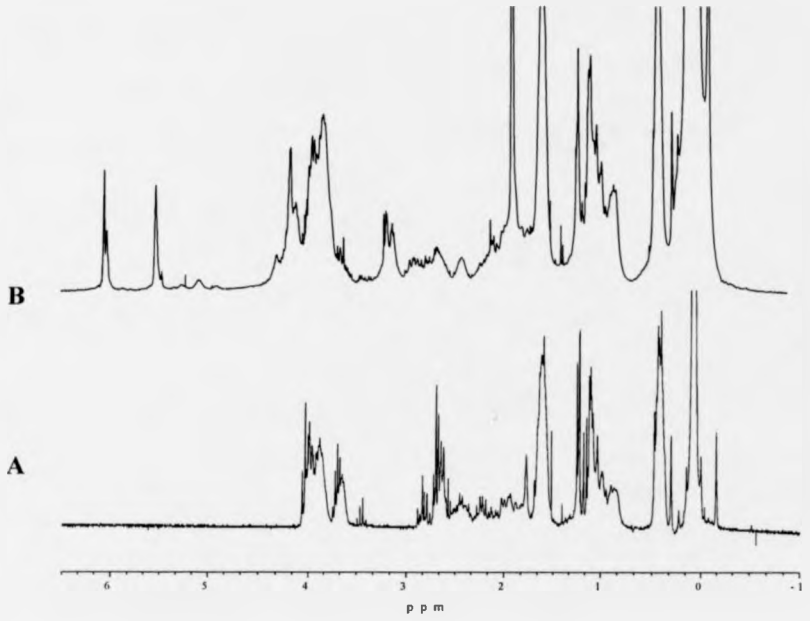

Figure 4.9, ^{1}H NMR in $CDCl_3$ of **A)** hydroxyl functional poly(TRIS) showing the O**CH$_2$** (3.75-4.12 ppm), α-S**CH$_2$** (2.52-2.75 ppm), α-**CH$_2$**OH (3.55-3.75 ppm) and **CH$_2$**Si (0.32-0.58 ppm) **B)** after reaction with isocyanatoethyl methacrylate the presence of the vinylic protons at 5.55-5.60 ppm and 6.07-6.13 ppm and the appearance of the α-O**CH$_2$** protons at 4.08-4.25 ppm

4.2.2 Conclusion

In agreement with the findings of McGee and Valint macromonomers of TRIS were prepared using functional mercaptan chain transfer agents. However, as discussed earlier in this chapter there are problems with initiation and termination steps that are responsible for a fraction of the chain ends and thus not 100 % of the oligomers contain vinyl functionality. There are also problems associated with the toxicity of the mercaptans and the stringent cleaning procedures required if the process is to be

developed to industrial scale. Whilst in this example the polydispersity of the samples are low ordinarily broader molecular weight distributions are observed with polydispersity indexes of ~2 as would be expected if higher molecular weight oligomers were prepared by this method.

4.3 Transition Metal Mediated Living Radical Polymerisation

As discussed TMM-LRP is a relatively recent development in the area of controlled polymerisation and its arrival has allowed great control over α-terminal functionality. The mechanism through which TMM-LRP functions results in polymer with 100 % α-terminal functionality corresponding to the structure of the initiator used. With an almost inexhaustible supply of alkyl halide initiators being applicable, TMM-LRP is an appropriate technique for the formation of telechelic materials. A communication from Haddleton *et al.* describes the use of 2-hydroxyethyl 2'-methyl-2'-bromopropionate (*figure 4.10* **A**) as initiator in the TMM-LRP of MMA using a copper(I) *N-n*-propyl-2-pyridylmethanimine complex to prepare monohydroxy α-terminal functional PMMA[10]. It was shown that control over molecular weight and polydispersity was not affected detrimentally by the presence of the primary alcohol group. In fact the polymer had a narrower MWD and the rate of polymerisation was faster than with the standard non-functional initiator. Similarly Coessens and Matyjaszewski reported the preparation of monohydroxy α-terminal functional polystyrene using 2-hydroxyethyl 2'-bromopropionate (*figure 4.10* **B**) as initiator and a CuBr-bipyridine complex as catalyst[11].

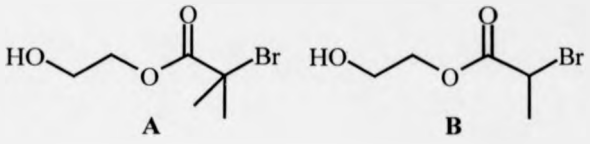

Figure 4.10, Structures of 2-hydroxyethyl 2'-methyl-2'-bromopropionate (**A**) and 2-hydroxyethyl 2'-bromopropionate (**B**) used in the Preparation of α-hydroxyl functional PMMA and Polystyrene

It follows that as with the hydroxyl α-terminal functional polymer produced using mercaptoethanol it would be possible to react the hydroxyl group of a polymer prepared by the method described by Haddleton *et al.* with isocyanatoethyl methacrylate to produce the corresponding macromonomer. Alternatively an initiator containing a polymerisable unsaturated bond could be used to produce macromonomers by TMM-LRP. This would be beneficial, as it would eliminate the need for conversion of the hydroxyl group simplifying the procedure for macromonomer production. Nakagawa and Matyjaszewski have reported the use of allyl bromide and allyl chloride (*figure 4.11* **C**) as initiators in the polymerisation of styrene using CuBr-bipyridine complex as catalyst at 100 °C and 130 °C respectively[12]. Their results showed that there were no significant termination reactions, nor any significant transfer reactions during the polymerisation and the resultant polymers had relatively narrow MWDs (PDI 1.2 for allyl bromide). They concluded that both allyl bromide and allyl chloride are efficient initiators in TMM-LRP and that resultant polymers contained 100 % allyl functionality. Matyjaszewski and co-workers have also examined the use of (*figure 4.11* **C, D & E**) initiators under similar polymerisation conditions with similar results as for the polymerisation with allyl bromide[13].

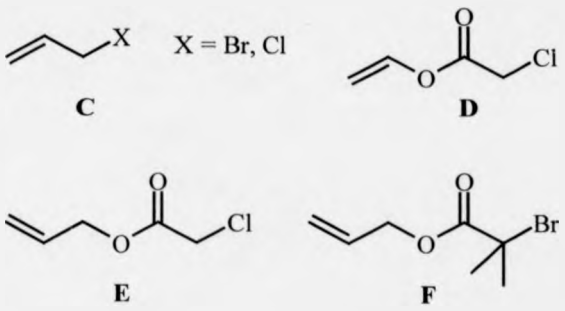

Figure 4.11, Initiators used in TMM-LRP to produce macromonomers, allyl bromide/chloride (**C**), vinyl 2'-chloropropionate (**D**), allyl 2'-chloropropionate (**E**) and allyl 2'-methyl-2'-bromopropionate (**F**)

The benefits of employing TMM-LRP to the production of macromonomers include 100 % α-terminus functionality, narrow MWD and good control over molecular weight (determined by the ratio of monomer to initiator).

Prior to discussing the production of low molecular weight macromonomers it needs to be shown that TMM-LRP is applicable to TRIS and that it works effectively, *i.e. living/controlled* polymerisation. This is important when we consider the problems that were observed in CCTP of this monomer due to the presence of oxygen that could not be removed through routine methods of deoxygenating. To do this a series of polymerisations was carried out under various polymerisation conditions using copper (I) *N-n*-alkyl-2-pyridylmethanimine complexes. If the polymerisation is indeed *living* then the first-order rate plot (ln $[M]_0/[M]$ vs. time) should be linear and pass through the origin, indicating that the concentration of active species is constant throughout the reaction, and the polydispersity should be low. There should also be an increase in the number average molecular weight relative to conversion defined by *equation 4.4*,

$$Mn_{theo} = \frac{\text{Conversion}(\%)}{100} \frac{[M]_0}{[In]_0} F.W._M + F.W._{Init} \qquad \textbf{(4.4)}$$

Where, $[M]_0$ and $[In]_0$ are the initial concentrations of monomer and initiator respectively, and $F.W._M$ and $F.W._{Init}$ are the molecular weights of the monomer and initiator respectively.

4.3.1. Results and Discussion

Polymerisations of TRIS were carried out in toluene (70 % v/v) at 90 °C with various initiators. Preliminary reactions with standard ratios of [Cu(I)Br] : [Ligand] (*Lig*): [Initiator] (*Init*): [TRIS] (*i.e.* 1:2:1:100 and 1:2:1:60) yielded no polymer. It was noted that the solutions became heterogeneous in the first few minutes of the polymerisation forming a black tar like substance at the base of the reactor. The ligand used in the first set of polymerisations was the less soluble *N*-*n*-propyl-2-pyridylmethanimine (*^{n}Pr*) which is not completely soluble under the conditions and it was considered that this could be the reason for the lack of polymerisation. Reactions were repeated with the more soluble *N*-*n*-octyl-2-pyridylmethanimine (*^{n}Oc*) however, this produced identical results. If oxygen is present in the system at high enough concentrations there are two possible explanations for the observed results. The first is the termination of radical species by the oxygen thus initiation does not occur. The second is the formation of deactivating Cu(II) which at high concentrations may be sufficient to inhibit polymerisation. To test this theory two series of polymerisations were carried out with increased levels of Cu(I)Br and ligand. Alternatively the addition of Cu(0) would have a similar effect as it would reduce Cu(II) back to Cu(I)

however this has not been explored for this system. In the first series (A1-3) the effect of increasing the ratio of Cu(I)Br : *Init* from 1:1 to 2:1, 3:1 and 4:1 was investigated. In the second series (B1-4) even higher concentrations of Cu(I)Br (Cu : *Init*, 5:1 and 10:1) were examined using both ethyl-2-bromoisobutyrate (**G**) and 2-hydroxyethyl 2'-methyl-2'-bromopropionate initiators (**A**). The reaction conditions for these polymerisations are outlined in *table 4.8* and the rate plots and dependence of *Mn* on conversion graphs are shown in *figures 4.12-4.16*. Molecular weight information was obtained from SEC using *Mark-Houwink* constants appropriate to PMMA.

Table 4.8, Experimental data for TMM-LRP of TRIS in Toluene (70 % v/v) at 90 °C under Various Conditions. Initiators (*Init*) employed are outlined in *figures 4.9 & 4.10.*

	Lig	*Init*	[TRIS]/ [*Init*]	[Cu]/ [*Init*]	Time (mins)	Conv. (%)	*Mn* (theory)	*Mn* (SEC)	PDI
A1	*nPr*	**A**	60	4	360	63.7	16200	14200	1.12
A2	*nPr*	**A**	60	3	360	58.5	14900	15000	1.10
A3	*nPr*	**A**	60	2	360	37.5	9570	9370	1.10
B1	*nOc*	**G**	100	10	360	78.4	33200	20500	1.18
B2	*nOc*	**G**	100	5	360	42.3	17900	12400	1.11
B3	*nOc*	**A**	100	10	360	62.4	26400	24300	1.15
B4	*nOc*	**A**	100	5	360	57.3	24200	14800	1.36

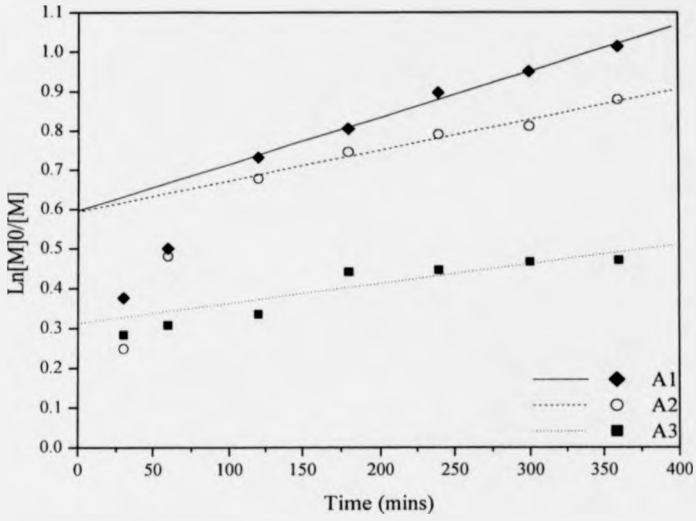

Figure 4.12, Rate plots for TMM-LRP of tris(trimethylsiloxy)-3-methacryloxy propylsilane (70 % v/v toluene at 90 °C, [TRIS]:[**A**]:[CuBr]:[^{n}Pr], A1 = [60]:[1]:[4]:[8], A2 = [60]:[1]:[3]:[6], A3 = [60]:[1]:[2]:[4])

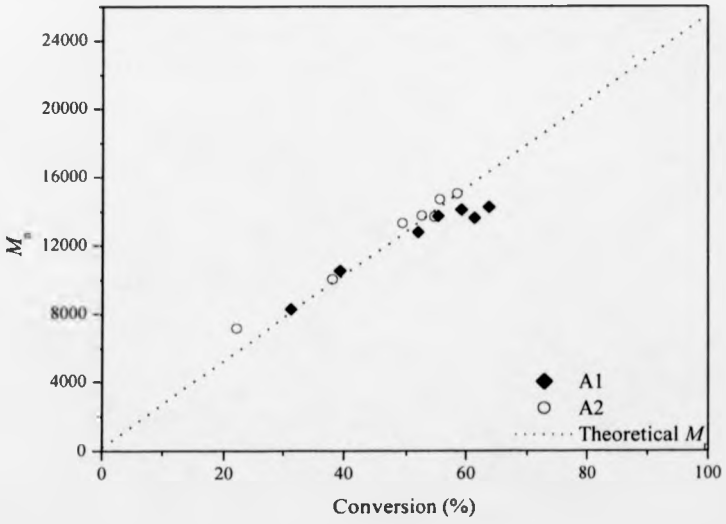

Figure 4.13, Dependence of *Mn* on conversion for TMM-LRP of Tris(trimethylsiloxy)-3-methacryloxy propylsilane (70 % v/v Toluene at 90 °C, [TRIS]:[**A**]:[CuBr]:[^{n}Pr], A1 = [60]:[1]:[4]:[8], A2 = [60]:[1]:[3]:[6])

The rate plots for reactions A1-3, *figure 4.12*, are not linear indicating that the concentration of radicals is varying with time. The reaction containing double the concentration of copper (A3) shows an initial period of rapid polymerisation and at 30 mins has reached 24.7 % conversion, the rate of the reaction then dramatically reduces and conversion only reaches 37.5 % after 6 hours. Whilst there is an increase in *Mn* with conversion it is not linear and the plot is fairly erratic, however the PDI of the final product (at 6 hours) is low at only 1.10. The rates of polymerisation for reactions A1 and A2 are fast at the beginning and slowly tail off, after 2 hours the rates appear to become linear, conversion at this time is fairly low at ~50 %. This can be explained by considering the ratios of Cu(I) and Cu(II) present in the system. Initially the level of Cu(I) will be high and the level of Cu(II) low. Any oxygen present may oxidise the Cu(I) to Cu(II). This will have the effect of increasing the Cu(II) concentration whilst decreasing the Cu(I) concentration. This would result in a decrease in the rate of polymerisation. From *figure 4.13* we see that *Mn* is dependent upon conversion, closely following the theoretical line, and from *table 4.8* we see that the polydispersities are low. This indicates that chain transfer and termination reactions are negligible.

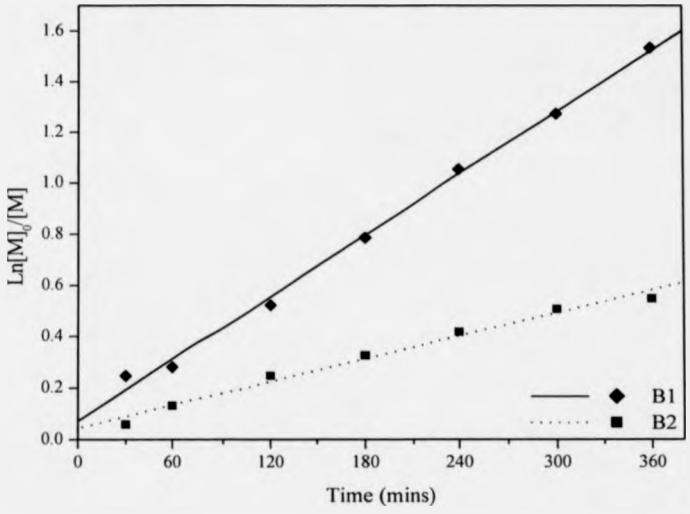

Figure 4.14, Rate Plots for TMM-LRP of Tris(trimethylsiloxy)-3-methacryloxy propylsilane (70 % v/v Toluene at 90 °C, [TRIS]:[**G**]:[CuBr]:[^{n}Oc], B1 = [100]:[1]:[10]:[20], B2 = [100]:[1]:[5]:[10])

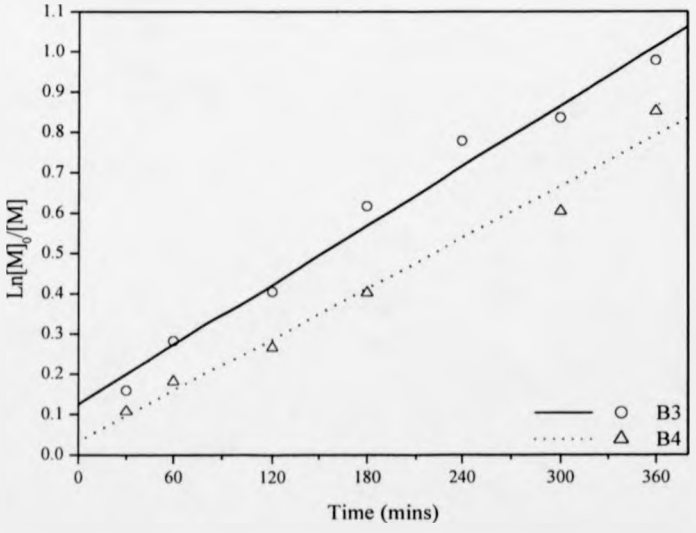

Figure 4.15, Rate plots for TMM-LRP of Tris(trimethylsiloxy)-3-methacryloxy propylsilane (70 % v/v Toluene at 90 °C, [TRIS]:[**A**]:[CuBr]:[^{n}Oc], B3 = [100]:[1]:[10]:[20], B4 = [100]:[1]:[5]:[10])

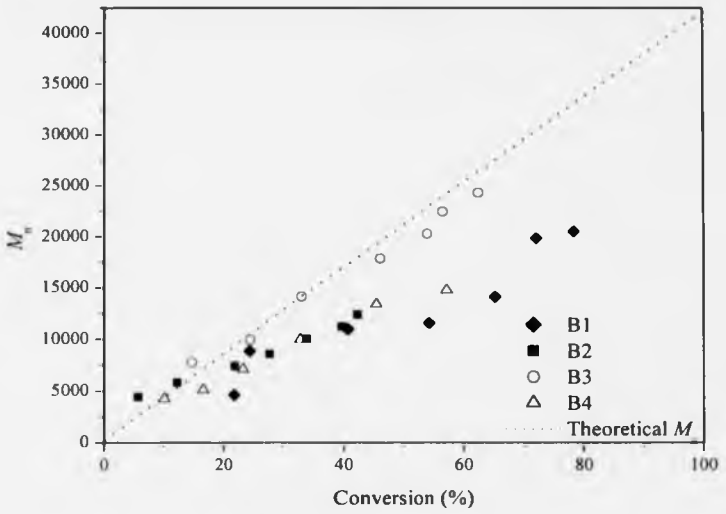

Figure 4.16, Dependence of *Mn* on conversion for TMM-LRP of Tris(trimethylsiloxy)-3-methacryloxy propylsilane (70 % v/v Toluene at 90 °C, [TRIS]:[*Init*]:[CuBr]:[^{n}*Oc*], B1 & B3 = [100]:[1]:[10]:[20], B2 & B4 = [100]:[1]:[5]:[10])

The series of polymerisations B1-4 were left for a longer period before the polymerisation was initiated. This would have the effect of addressing the balance between Cu(I)/Cu(II) prior to the start of the polymerisation. The rate plots for these polymerisations are linear and polydispersity indexes are low (~1.2). However, with the exception of reaction B3 the *Mn* does not hold to the theoretical *Mn* with conversion although there is a linear relationship between *Mn* and conversion. It is noted that the molecular weight information obtained from SEC has been calculated using *Mark-Houwink* parameters appropriate to PMMA and not TRIS. Using the *Mark-Houwink* parameters for TRIS measured by Muratore *et al.* to calculate the molecular weights we get an alternative perspective and observe that in all four cases the molecular weights are higher than the theoretical[1]. We should consider that if the

concentration of Cu(I) is high and the concentration of Cu(II) is low then there will be a high concentration of radicals at the beginning of the polymerisation. This would have the effect of increasing the probability of termination reactions occurring at the beginning of the reaction. Thus reducing the number of theoretical chains, causing an increase in molecular weight above the theoretical *Mn*. However this would also lead to an increase in PDI which is not observed. Having demonstrated that in principal TMM-LRP can be used to produce narrow molecular weight polymers with a targeted molecular weight, the next step was its application to produce the desired oligomeric species. Several experiments were conducted with higher levels of initiator; the reaction conditions are outlined in *table 4.9*.

Table 4.9, TMM-LRP of TRIS in Toluene (70 % v/v) at 90 °C under Various Conditions. Initiators (*Init*) employed are outlined in *figures 4.9 and 4.10*

	Lig	*Init*	[TRIS]/ [*Init*]	[Cu]/ [*Init*]	Time (mins)	Conv. (%)	*Mn* (theory)	*Mn* (SEC)	PDI
C1	*^{n}Oc*	**G**	24	8	120	86.6	9150	8610	1.27
C2	*^{n}Oc*	**G**	24	2	300	80.1	8460	6500	1.31
D1	*^{n}Oc*	**A**	5	0.5	300	86.2	2030	3700	1.14
D2	*^{n}Pr*	**A**	5	0.5	300	84.2	1990	3510	1.14
E1	*^{n}Oc*	**F**	6	0.5	300	81.7	2280	4240	1.18
E2	*^{n}Pr*	**F**	6	0.5	300	81.0	2260	3770	1.14

The rate plots for reaction C1 and C2 are shown in *figure 4.17*, it is obvious that the rate plot for reaction C1 is curved. This is explained by the high conversion of 86.6 % that is reached in just 2 hours, therefore monomer concentration is low and a reduction in rate is observed. It is presumed that the fast rate of this polymerisation is due to the high level of Cu(I)Br employed. If the presence of oxygen in these

polymerisation systems is the reason for the results observed then it follows that the level of Cu(I)Br needed to achieve controlled polymerisation is independent of initiator concentration but instead dependent on the level of oxygen present in the system. Therefore, the ratio of Cu(I)Br to initiator can be reduced when the ratio of initiator to monomer is increased. With a ratio of Cu(I)Br / *Init* of 2:1 and TRIS / *Init* of 24:1, reaction C2, the rate plot was linear and molecular weight increased linearly with conversion, *figure 4.18*.

This indicates that the polymerisation is living although the PDI of 1.31 suggests chain transfer or termination occurs to some extent. This is most probably due to termination reactions occurring at the beginning of the polymerisation when Cu(II) concentrations are low and therefore radical lifetimes are higher.

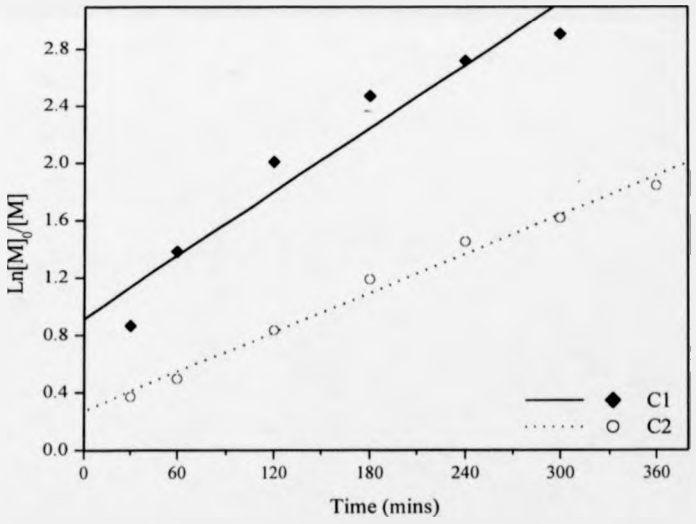

Figure 4.17, Rate plots for TMM-LRP of tris(trimethylsiloxy)-3-methacryloxy propylsilane (70 % v/v toluene at 90 °C, [TRIS]:[**G**]:[CuBr]:[*"Oc*], C1 = [24]:[1]:[8]:[16], C2 = [100]:[1]:[2]:[4])

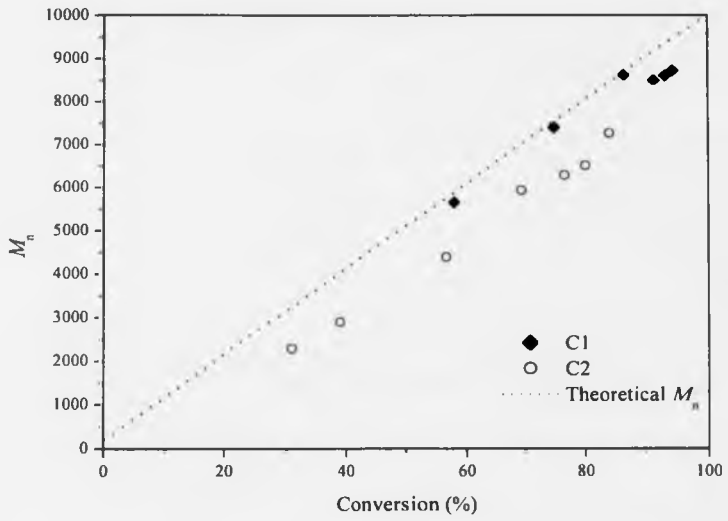

Figure 4.18, Dependence of *Mn* on conversion for TMM-LRP of Tris(trimethylsiloxy)-3-methacryloxy propylsilane (70 % v/v Toluene at 90 °C, [TRIS]:[**G**]:[CuBr]:[^{n}*Oc*], C1 = [24]:[1]:[8]:[16], C2 = [24]:[1]:[2]:[4])

When even higher concentrations of initiator ([TRIS]:[*Init*] ~5:1) were employed it was not surprising to find that with increased Cu(I)Br concentrations, as compared to standard conditions, the polymerisations were uncontrolled, *i.e.* fast rate of reaction, high polydispersity indexes and higher than theoretical molecular weights. However, controlled reactions were achieved when a Cu(I)Br/*Init* ratio of 1:0.5 was used. Four similar reactions were carried out using either a hydroxyl (**A**, reactions D1&2) or allyl (**F**, reactions E1&2) functional initiator. The rate plots for these reactions are shown in *figures 4.19 & 4.20* and it can be seen that they are linear. *Figures 4.21 & 4.22* show the dependence of *Mn* on conversion for reactions D1&2 and E1&2 respectively and it can be seen that for all four reactions molecular weights are higher than the theoretical molecular weights. An explanation for this is that of the persistent radical

effect (*section 1.6.3.5*) and the very high levels of initiator with respect to monomer that have been employed in this example. At the onset of the polymerisation the level of deactivating Cu(II) is zero and so the rate of deactivation is far slower than the rate of termination therefore, termination reactions between initiating species occur and the observed molecular weight of resultant polymer will be higher than the theoretical. In this example the radical concentration is higher than in a typical TMM-LRP reaction because of the high concentration of initiator and therefore, a greater difference in the theoretical and the observed *Mn* is expected.

However, molecular weights increase linearly with conversion and the molecular weight distributions of the polymers are narrow (PDIs ~ 1.14) suggesting that the polymerisation is living and chain transfer and termination reactions are insignificant.

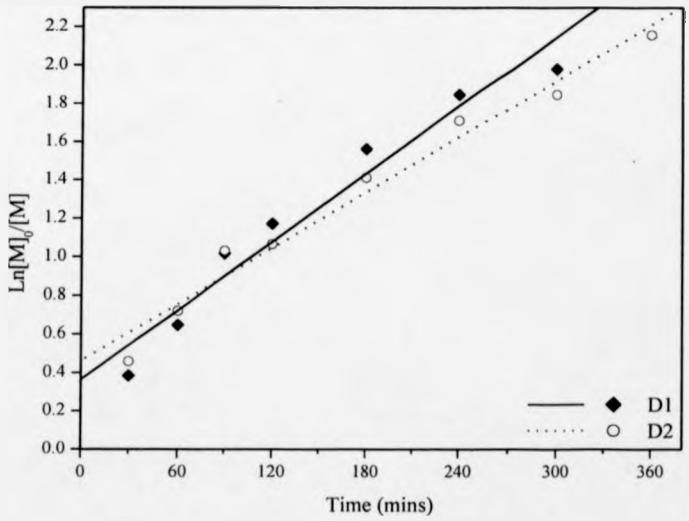

Figure 4.19, Rate plots for TMM-LRP of tris(trimethylsiloxy)-3-methacryloxy propylsilane (70 % v/v toluene at 90 °C, [TRIS]:[**A**]:[CuBr]:[*Lig*], D1 and D2 = [5]:[1]:[0.5]:[1]

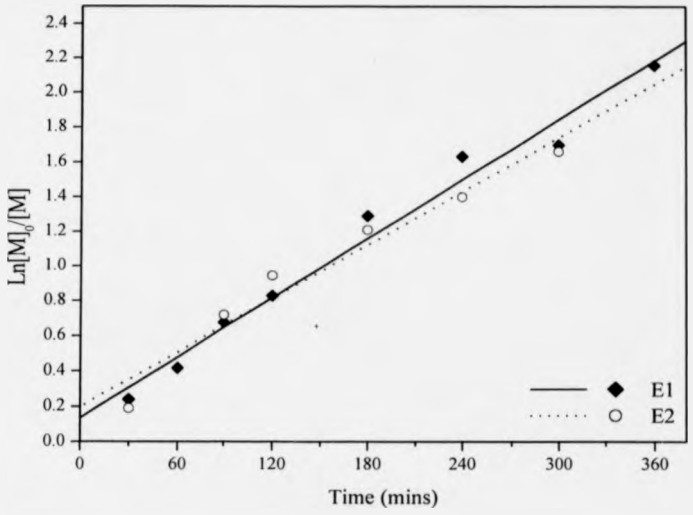

Figure 4.20, Rate plots for TMM-LRP of tris(trimethylsiloxy)-3-methacryloxy propylsilane (70 % v/v toluene at 90 °C, [TRIS]:[**F**]:[CuBr]:[*Lig*], E1 and E2 = [6]:[1]:[0.5]:[1]

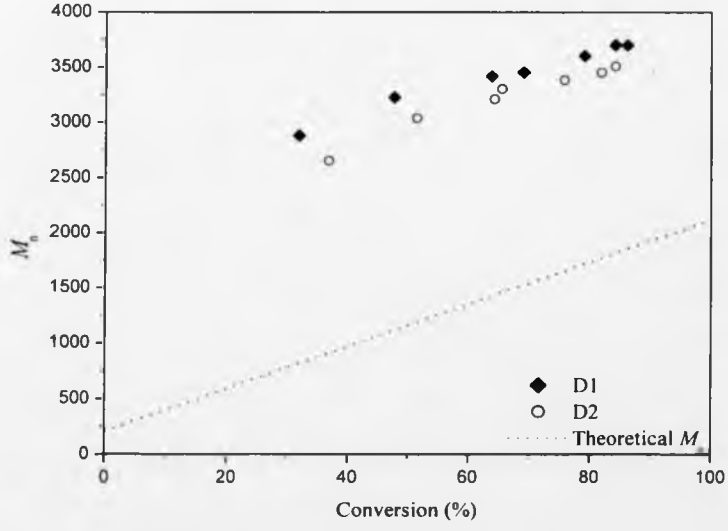

Figure 4.21, Dependence of *Mn* on conversion for TMM-LRP of Tris(trimethylsiloxy)-3-methacryloxy propylsilane (70 % v/v Toluene at 90 °C, [TRIS]:[**A**]:[CuBr]:[*Lig*], D1 and D2 = [5]:[1]:[0.5]:[1]

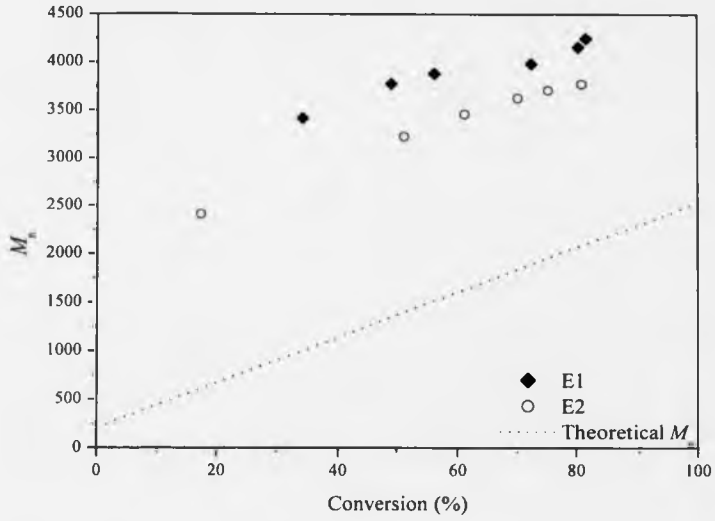

Figure 4.22, Dependence of *Mn* on conversion for TMM-LRP of Tris(trimethylsiloxy)-3-methacryloxy propylsilane (70 % v/v Toluene at 90 °C, [TRIS]:[**F**]:[CuBr]:[*Lig*], E1 and E2 = [6]:[1]:[0.5]:[1]

4.3.2 Conclusion

The application of TMM-LRP to the polymerisation of TRIS is not without problems. It is proposed that due to the high affinity for oxygen that TRIS exhibits trace levels of oxygen are still present after routine freeze, pump, thaw deoxygenating and that this causes an increase in the levels of Cu(II) resulting in a reduction in rate. However, it has been shown that by using higher levels of Cu(I)Br living polymerisation can be achieved. The production of low molecular weight oligomers has also been demonstrated however, molecular weights are believed to be greater than would be expected from the ratio of monomer to initiator used. This is most probably due to bimolecular termination reactions at the beginning of the polymerisation. An

alternative method of oligomer production would be to use a lower level of initiator and terminate the reactions at low conversion. However, unless an efficient method of monomer recycling could be achieved given the high cost of TRIS this would not be financially viable.

4.4 Preparation of TRIS Macromonomers by TMM-LRP

Having demonstrated the applicability of TMM-LRP to the production of oligomers of TRIS two oligomers were prepared with differing α-functionality. The first using 2-hydroxyethyl 2'-methyl-2'-bromopropionate (**A**) to give an oligomer with a terminal hydroxyl functional group which was subsequently reacted with isocyanatoethyl methacrylate to produce a macromonomer. The second polymer was produced using allyl 2'-methyl-2'-bromopropionate (**F**) to give an oligomer with the corresponding terminal vinyl functionality.

4.4.1 Results and Discussion

TMM-LRP of TRIS using 2-hydroxyethyl 2'-methyl-2'-bromopropionate (**A**) as initiator with *N*-*n*-propyl-2-pyridylmethanimine and CuBr was carried out at 90 °C in toluene [TRIS]:[*Init*]:[*Lig*]:[CuBr], [10]:[2]:[2]:[1]. The polymerisation was stopped after 4 hours (82.4 % conversion by NMR) to reduce the amount of termination by radical-radical reactions. The polymer was purified by passing over basic alumina to remove the copper catalyst and rotary evaporation of the solvent. The polymer was then dissolved in chloroform and subsequently precipitated from a 10-fold excess of ice cold methanol before being placed under high vacuum for 24 hours (3×10^{-2}

mbar). A monomer : initiator ratio of 5:1 was used giving a theoretical *Mn* of 2400 at 100 % conversion. The *Mn* obtained from SEC using *Mark-Houwink* parameters appropriate to PMMA was 3000, PDI = 1.19, the *Mn* has also been calculated through ^{1}H NMR analysis to be 1700 which is considerably lower than the SEC result however it corresponds well with the theoretical *Mn* of 1980 at the conversion reached.

In this instance ^{1}H NMR analysis is of little assistance in confirming the quantitative presence of the hydroxyethyl ester group as the resonances of the α-$CO_2\mathbf{CH_2}$ and α-$\mathbf{CH_2}$OH protons are obscured by the significantly larger $CO_2\mathbf{CH_2}$ resonance lying between 3.74-4.32 ppm, see *figure 4.24* **A**. The α-CO_2CH_2 resonance can be seen protruding from the main peak between 4.02-4.32 ppm.

The α-terminal hydroxyl functional polymer was reacted with isocyanatoethyl methacrylate to produce a TRIS macromonomer with low polydispersity, see *figure 4.23*, the reaction was carried out as previously described in *section 4.1.3*.

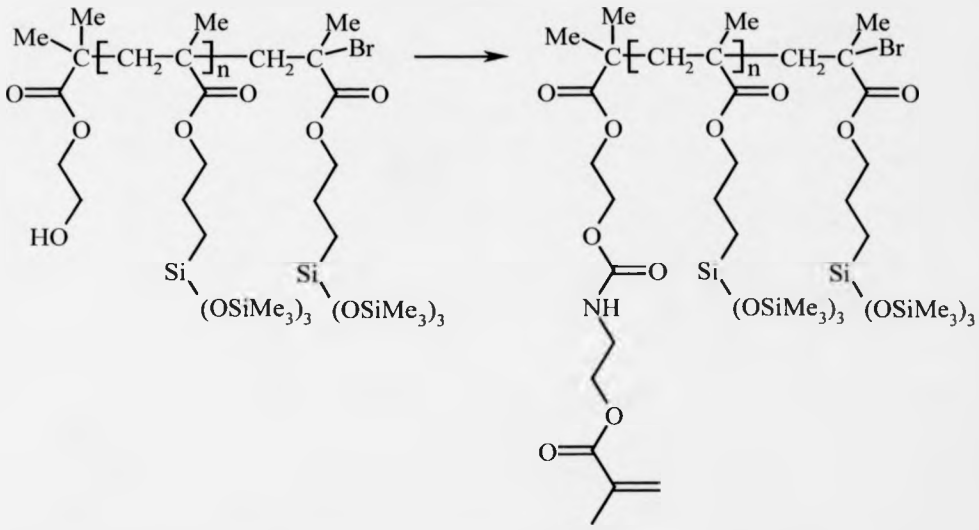

Figure 4.23, Reaction of hydroxyl functional PolyTRIS prepared by TMM-LRP with isocyanatoethyl methacrylate in the presence of dibutyltin dilaurate and the inhibitor 2,6-Di-*tert*-butyl-4-methylphenol

^{1}H NMR analysis confirms the presence of the characteristic vinyl protons at 5.50-5.55 ppm and 6.04-6.13 ppm, see *figure 4.24* **B**. The presence of resonances of the α-CO_2**CH_2CH_2**CO_2NH at 4.0-4.3 ppm, α-**NH** at 4.78-4.98 ppm, α-NH**CH_2** at 3.50-3.65 ppm and α-$NHCH_2$**CH_2**CO_2 at 3.29-3.50 ppm confirms the reaction between the isocyanate and the hydroxyl group. Through comparison of the vinylic proton resonance and that of the **CH_2**Si of TRIS at 0.27-0.51 ppm and the CO_2**CH_2** of TRIS at 3.72-4.06 ppm the *Mn* of the polymer has been calculated to be 1920. This is a lot lower than the value for *Mn* of 3500, PDI 1.11 obtained through SEC but agrees well with the *Mn* calculated by NMR of the hydroxyl functional polymer, and shows there to be quantitative coupling.

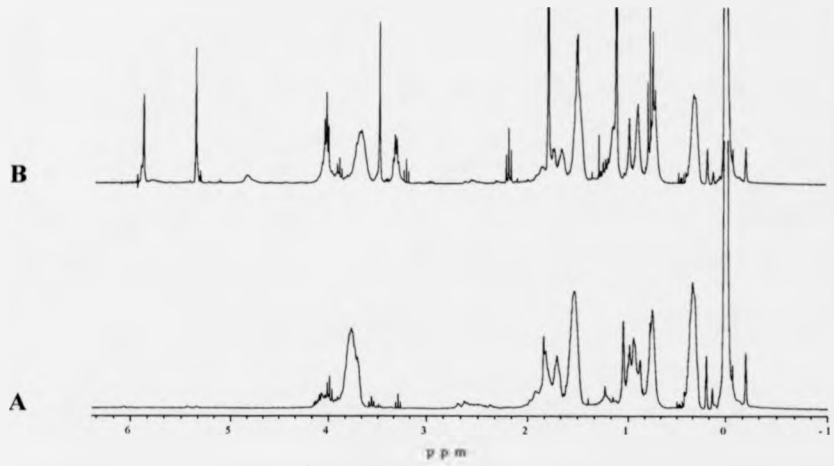

Figure 4.24, Section of the ^{1}H NMR in $CDCl_3$ of **A)** hydroxyl functional poly(TRIS) showing the protons of α-CO_2**CH_2**, CO_2**CH_2** and α-**CH_2**OH groups between 3.74-4.32 ppm **B)** after reaction with isocyanatoethyl methacrylate the presence of the vinylic protons at 5.50-5.55 ppm and 6.04-6.13 ppm, and the appearance of the following resonances: α-CO_2**CH_2CH_2**CO_2NH at 4.0-4.3 ppm, α-**NH** at 4.78-4.98 ppm, α-NH**CH_2** at 3.50-3.65 ppm and α-NHCH_2**CH_2**CO_2 at 3.29-3.50 ppm

TMM-LRP of TRIS using allyl 2'-methyl-2'-bromopropionate (**F**) as initiator was conducted as described in *section 4.4.1* for TMM-LRP of TRIS using 2-hydroxyethyl 2'-methyl-2'-bromopropionate. The polymerisation was stopped after 2 hours (62 % conversion by ^{1}H NMR) to reduce the amount of termination by radical-radical reactions. The polymer was purified by passing over basic alumina to remove the copper catalyst and isolated by removal of volatiles in vacuo. The polymer was then dissolved in chloroform and subsequently precipitated from a 10-fold excess of ice cold methanol before being placed under high vacuum for 24 hours (3×10^{-2} mbar). A monomer : initiator ratio of 6:1 was used giving a theoretical *Mn* of 2700 at 100 % conversion. The *Mn* obtained from SEC using *Mark-Houwink* parameters appropriate

to PMMA was 3460, PDI = 1.13, the *Mn* has also been calculated through ^{1}H NMR analysis to be 3620 which corresponds well with the SEC results. This is significantly higher than the theoretical *Mn* of 1760 at the conversion reached. The ^{1}H NMR spectrum of the precipitated polymer is shown in *figure 4.25*. The presence of resonances of the α-OCH_2**CH**CH_2 at 5.68-5.90 ppm, α-OCH_2CH**CH_2** at 5.01-5.31 and α-**OCH_2**$CHCH_2$ at 4.29-4.51 ppm clearly show that the allyl group is covalently attached to the polymer and has not participated in the polymerisation to any significant extent.

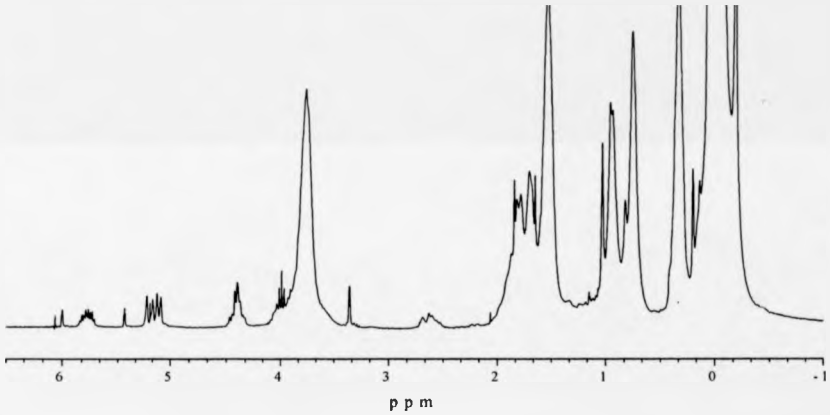

Figure 4.2.5, Section of the ^{1}H NMR in $CDCl_3$ of allyl functional poly(TRIS) prepared by TMM-LRP showing the resonances of the α-OCH_2**CH**CH_2 at 5.68-5.90 ppm, α-OCH_2CH**CH_2** at 5.01-5.31 and α-**OCH_2**$CHCH_2$ at 4.29-4.51 ppm

4.4.2 Conclusions

TMM-LRP has been shown to be a new reliable method for the production of macromonomers. The products having well-controlled molecular weights, being a

function of the ratio of monomer to initiator, and low polydispersity. This method of macromonomer production also has the benefit of 100 % terminal functionality.

4.6 References

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Chapter 5

Controlled Polymerisation of 2-(Methacrylocyethyl)-2'-(trimethylammoniumethyl) phosphate

5 Controlled Polymerisation of 2-(Methacryloxyethyl) -2'-(trimethylammoniumethyl)phosphate

The use of polymers containing phosphoryl choline (PC) functionality to improve biocompatibility of biological devices including contact lenses is receiving increased interest, *section 2.4.2*. The majority of the published research has concentrated upon the application of these polymers with only a few publications dealing with the polymerisation techniques used. This chapter examines methods of producing macromonomers of 2-(methacryloxyethyl)-2'-(trimethylammoniumethly)phosphate (HEMA-PC) a phosphoryl choline containing methacrylate monomer, *figure 5.1*. Contact lenses formed from a copolymer of HEMA-PC and HEMA have been commercially available for some time under the trade name Proclear™.

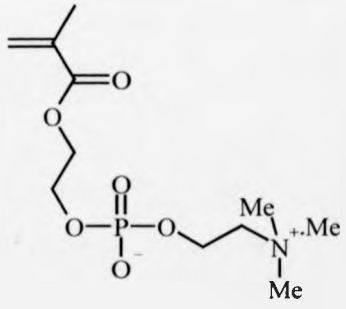

Figure 5.1, Structure of the phosphoryl choline containing methacrylate monomer 2-(methacryloxyethyl)-2'-(trimethylammoniumethyl)phosphate

5.1 Chain Transfer Polymerisation

The use of chain transfer agents such as mercaptans to limit molecular weight and/or introduce end group functionality has been recognised for some time. Ishihara *et al.* reported the use of mercaptoacetic acid in the free radical polymerisation of HEMA-PC and subsequent reaction of the carboxylic acid end group with glycidyl methacrylate to form macromonomers[1]. They reported the production of three such macromonomers with various molecular weights. In order to reproduce the results of Ishihara *et al.* a series of polymerisations was carried out with differing levels of mercaptan. From these results a *Mayo-plot* was produced enabling the production of polymers with a specific molecular weight through predetermining the level of mercaptan required. Once the level of mercaptoacetic acid required was established the polymerisations were scaled up and the products of these reactions reacted with glycidyl methacrylate to produce the corresponding macromonomers.

5.1.1 Results and Discussion

The polymerisations of HEMA-PC were carried out in ethanol (70 % w/w) with AIBN (0.12 mol %) in the presence of mercaptoacetic acid at various levels. The solutions were deoxygenated via three consecutive freeze, pump, thaw cycles prior to heating to 60 °C for 24 hours. ^{1}H NMR analysis of these solutions showed that near complete conversion had been reached. The polymers, dissolved in ethanol, were purified by three successive precipitations from a 10 fold excess of diethyl ether. The polymer was isolated by filtration and volatiles removed in vacuo. Molecular weight information was obtained through potentiometric titration of the carboxylic acid end

group. Titrations were carried out through slow addition of KOH solution, with known concentration, to a solution of the polymer, of known concentration containing phenolphthalein. After a change in colour was observed an excess of the KOH solution was added and then the solution was back-titrated with HCl solution of known concentration. Again after colour transition had occurred an excess of the acid was added and then a final titration with KOH solution was carried out. The quantities of solution added were recorded and from this data the level of acid present in the polymer was calculated allowing evaluation of the *Mn* of the polymers. The levels of mercaptan, molecular weight and conversion data for the polymerisations are tabulated below, *table 5.1*.

Table 5.1, Reaction Conditions and Molecular Weight/Conversion Data for Polymerisation of 2-(methacryloxyethyl)-2'-(trimethylammoniumethyl)phosphate in Ethanol at 60 °C in the Presence of Mercaptoacetic acid

	[Merc]/ [HEMA-PC] × 10^2	*Mn*	% Conversion	DP_n	$1/DP_n$
A1	2.12	6400	97.6	21.74	0.046
A2	4.95	3800	93.5	12.93	0.077
A3	7.08	3100	94.8	10.40	0.096
A4	12.03	2500	97.5	8.42	0.119
A5	24.07	1300	97.8	4.30	0.232

As discussed in *section 1.4.2.1*, the effectiveness of a chain transfer agent is given as the chain transfer constant, *Cs*, which can be calculated through manipulation of the *Mayo-equation*[2]. For an accurate calculation of the *Cs*, conversion should be minimised (typically < 10 %) because as the reaction proceeds both monomer and chain transfer agent are consumed at differing rates and thus the ratio of chain transfer agent to monomer will vary. In this example due to problems associated with

molecular weight determination and purification, polymerisations were taken to high conversions. Whilst the *Cs* value obtained will contain a larger associated error it will still facilitate accurate molecular weight prediction. From the slope of the pseudo *Mayo-plot* the apparent chain transfer constant of mercaptoacetic acid to HEMA-PC has been calculated to be $Cs = 0.822 \pm 0.05$, see *figure 5.2*. This value is in good agreement with *Cs* values reported for mercaptoacetic acid with other methacrylates such as MMA for which a $Cs = 0.63$ for the bulk polymerisation at 60 °C has been reported[3].

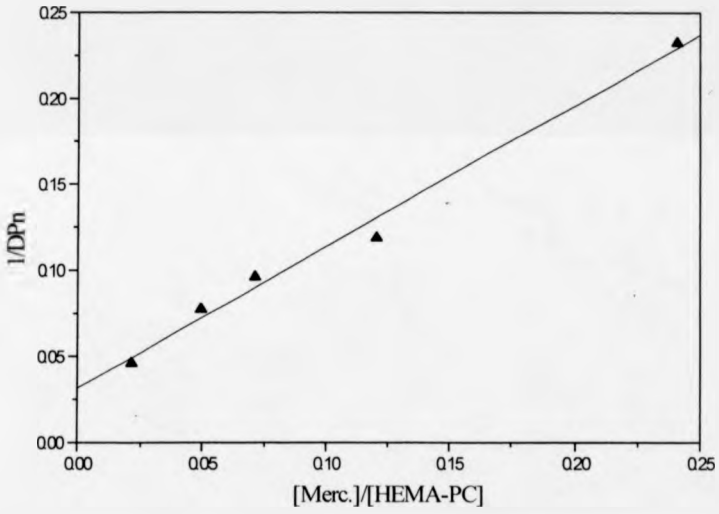

Figure 5.2, Pseudo *Mayo-plot* for the polymerisation of 2-(methacryloxyethyl)-2'-(trimethylammoniumethyl)phosphate in ethanol at 60 °C in the presence of mercaptoacetic acid; the apparent $Cs = 0.82$.

Information from the *Mayo-plot* was used to prepare two polymers with levels of mercaptoacetic acid to produce polymers with *Mn*s of 1150 and 2300 ([Merc]/[HEMA-PC] = 0.311 and 0.156 respectively). The polymerisations and

subsequent purification of the products were performed as above. Titration of the purified products confirmed the *Mn* of these polymers to be 1210 and 2430. ^{1}H NMR analysis of the reaction solution prior to purification showed that 94.6 % and 98.2 % conversion was reached respectively. From the ^{1}H NMR spectra of these polymers it is not possible to detect the presence of any of the end groups as they are obscured by the more abundant HEMA-PC OC**H$_2$**C**H$_2$**O proton resonances.

Coupling of the carboxylic acid functionalised polymers with glycidyl methacrylate was attempted under several conditions, see *figure 5.3*. Primarily the reaction outlined by Ishihara *et al.*[1] was followed, this simply involved heating (60 °C) the polymer in a solution of ethanol and glycidyl methacrylate for 16 hours. After reaction the polymers were purified by precipitation from a 10 fold excess of diethyl ether and dried under high vacuum (3×10^{-2} mbar) for 24 hours. ^{1}H NMR analysis at this time showed that no coupling had taken place. The reactions were repeated with the addition of a small quantity of N,N-dimethyldodecylamine as catalyst and a few mg's of 2,6-Di-tert-butyl-4-methylphenol as outlined in *section 4.2* for the production of TRIS macromonomers by the same route. However, again ^{1}H NMR analysis showed that the coupling reaction was unsuccessful. Subsequent reactions in anhydrous ethanol or 2-propanol were also unsuccessful. The coupling of the carboxylic acid with 2-hydroxyethyl methacrylate was also investigated. The use of 1-(3-dimethylaminopropyl)-3-ethyl-carbodiimide hydrochloride (EDCI) as a coupling reagent between alcohols and carboxylic acids dissolved in water/dioxane in the presence of phosphoryl groups has previously been demonstrated with high yields[4-6]. A 3-fold excess of EDCI and a 10-fold excess of HEMA were added to a solution of HEMA-PC dissolved in water/dioxane (50:50). The reaction was left for 48 hours before the polymer was precipitated from a 10 fold excess of diethyl ether and dried

under high vacuum (3×10^{-2} mbar) for 24 hours. ^{1}H NMR analysis was again used to determine the presence of any vinyl functionality within the polymer however, none was observed. A possible explanation for this apparent lack of reactivity of the carboxylic acid end group is the polymer's conformation in solution. It is feasible that in solution the acid end group of the polymer is inaccessible preventing the coupling reaction from occurring.

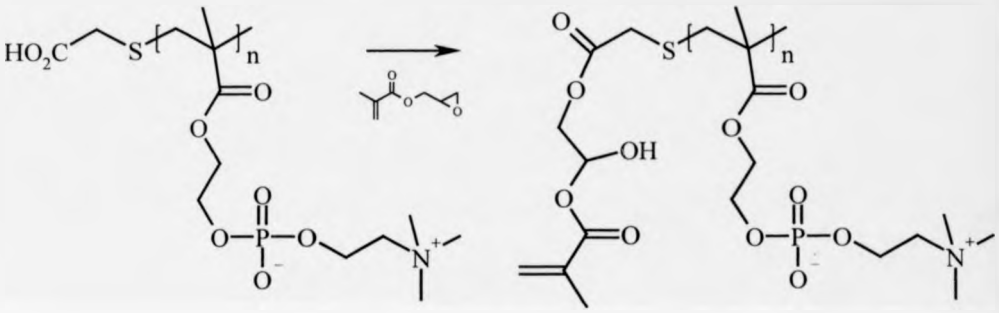

Figure 5.3, Preparation of HEMA-PC macromonomers through conversion of α-carboxylic acid end group

5.1.2 Conclusions

It has been shown that 2-mercaptoacetic acid is an effective chain transfer agent in the free radical polymerisation of HEMA-PC and that this method can be used to produce oligomeric species. However, subsequent coupling of the carboxylic acid functional group with either glycidyl methacrylate or 2-hydroxyethyl methacrylate was unsuccessful. Many functional mercaptans are available and there other coupling reactions that should be considered. For example, 2-aminoethanethiol hydrochloride or 2-mercaptoethanol could be used to introduce amine or hydroxyl functionality

respectively. Their reaction with an acid chloride, *i.e.* methacryloyl cholride, is facile with quantitative yields.

5.2 Catalytic Chain Transfer Polymerisation

5.2.1 Results and Discussion

5.2.1.1 Homopolymerisations

The second polymerisation technique applied to the polymerisation of HEMA-PC was that of CCTP. Initial results were inconclusive due to the solubility of poly(HEMA-PC). The only method of analysis available was by NMR spectroscopy. Whilst the cobalt catalyst may have had some effect on the polymerisation, the presence of any vinyl protons of the possible end group were not significant enough to show in the ^{1}H NMR spectra. This was true regardless of the levels of catalyst added to the polymerisations, which varied across a wide range up to, and including 8000 ppm. For the polymerisation of the majority of methacrylates, MMA for example, such high levels of catalyst would produce only oligomeric species the majority of which being dimer. Due to the complex functionality of the PC group it was suspected that the monomer was in some way deactivating the catalyst. Different cobalt complexes, active in CCTP, are known to have different chemical resistances. Therefore two other catalysts were tested, [Bis{μ-[diphenylethandione dioximate(2-)O:O']}tetrafluorodiborato(2-)-N,N',N'',N''']cobalt (CoPhBF) and [Bis{μ-[(1,2-cyclohexanedione dioximato)(2-)O:O']}tetrafluorodiborato(2-)-N,N',N'',N''']cobalt (NOXCoBF), see *figure 5.5*, however, the results were identical to those with CoBF.

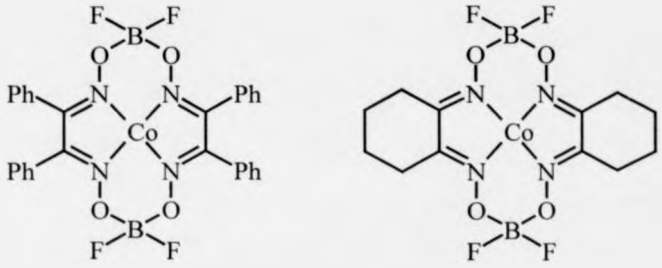

Figure 5.4, Structures of CoPhBF and NOXCoBF

The formation of complexes of phosphates with most metal ions including transition metal ions are well known and can be found in most modern inorganic texts[7]. A search of recent literature produces many references to the formation of various phosphorus-containing complexes for various applications. Examples include a recent publication giving evidence for direct co-ordination of a phosphoryl group to Ca^{2+} ion[8]. Phosphoryl-containing compounds have been shown to be effective in the extraction of various transition metals from nitric acid solutions[9] and water[10]. More significantly the synthesis of Cu(II), Co(II), Zn(II) and Ni(II) complexes with phosphoryl-containing ligands have been reported[11,12]. Considering this information it is most probable that co-ordination of the phosphoryl group in HEMA-PC to the Co(II) of the catalyst occurs to a significant extent. Given the ratio of catalyst to monomer there would be massive competition for the Co metal resulting in a much lower level of active cobalt catalyst (possibly zero) than added to the system. A common solution to the problem of catalyst poisoning is that of continually feeding the catalyst into the reactor throughout the polymerisation. Several experiments of this type were carried out with varying levels of CoBF. In one of these polymerisations ^1H NMR analysis revealed the presence of the characteristic vinylic protons of the end

group of the macromonomers produced through CCTP. ^{1}H NMR analysis gave a conversion of 12.2 % and the *Mn* was calculated at 8000.

The controlled polymerisation of acidic monomers such as methacrylic acid (MAA) and 2-aminoethyl methacrylate hydrochloride (AEMA) have, until recently, required the use of protecting group chemistry due to unwanted side reactions of these monomers with agents used in the polymerisations[13,14]. The low pH of these monomers in aqueous solution has also prevented the application of CCTP due to the deactivation of the cobalt complexes employed.

In 1996 Moad *et al.* described a novel procedure of producing macromonomers of HEMA via CCTP in aqueous solution using a feed system which gave high yields[15]. Recently Haddleton *et al.* successfully applied this method to the polymerisation of both MAA and AEMA to produce low molecular weight macromonomers[16]. This section discusses the application of this procedure to the synthesis of HEMA-PC macromonomers providing a more simple and effective route than the use of mercaptan chain transfer agents.

The polymerisation conditions are based upon those reported by Moad *et al.* for the polymerisation of HEMA[15]. However, in this case a cobalt(II) macrocycle, CoBF, instead of a cobalt(III)-alkyl was used. CoBF is useful as it is water soluble and the boron bridging groups increase, to some extent, hydrolytic stability. Typically HEMA-PC, 4,4'-azobis(4-cyano-pentanoic acid) (CVA) (8.5 wt %) and CoBF (at various levels) were dissolved in a mixture of water/methanol (78/24, 88 wt %) and subsequently heated to 80 °C. During the course of the reaction a solution of HEMA-PC and CoBF in water/methanol (64/36, 88 % w/w) was fed into the aqueous solution containing initiator over 1.5 hours. After 2 and 4 hours additional initiator (half the original quantity) was added and after 6 hours the reaction was quenched by

cooling. The polymers were isolated by rotary evaporation of the solvent and subsequently placing under vacuum in the presence of phosphorous pentoxide. Conversions and molecular weight data were calculated through ^{1}H NMR analysis, these are tabulated below alongside a summary of the reaction conditions, *table 5.2*. As can be seen from these results the conversions reached in just 6 hours are extremely high. This is in contrast to a typical CCTP evolving low molecular weight oligomers as the presence of the CoBF has been found to lower the rate of polymerisation[17,18].

Table 5.2, Reaction Conditions and Molecular Weight/Conversion Data for Polymerisation of 2-(methacryloxyethyl)-2'-(trimethylammoniumethyl)phosphate in Water/Methanol at 80 °C in the Presence of CoBF

	[CoBF]/ [HEMA-PC] × 10^6	*Mn*	DP_n	$1/DP_n$	% Conversion
B1	32.6	13510	45.77	0.02185	100.0
B2	50.4	8370	28.36	0.03526	97.0
B3	67.5	6240	21.13	0.04733	98.5
B4	84.2	4980	16.86	0.05931	100.0
B5	370.9	1510	5.10	0.19606	89.0

The *Mayo-plot* of the ratio of CoBF to HEMA-PC vs. $1/DP_n$ yields a value of 725 ± 3.4 for the *Cs* of this system, *figure 5.6*. This value is inaccurate as due to the nature of the polymerisation the ratio of catalyst to monomer is continually altering, however the value does allow accurate prediction of molecular weight for a given system. It should be noted that the *Cs* is some two orders of magnitude greater than that of 0.82 calculated for mercaptoacetic acid with this monomer. The *Cs* is significantly lower than those observed for solution or bulk polymerisations of other methacrylates such as MMA, where a chain transfer to monomer constant of 10000 in

methanol solution and 40000 for the bulk polymerisation at 60 °C are reported[19]. The much lower *Cs* obtained for this system is consistent with catalyst deactivation and compares well to the reported *Cs* of 1500 obtained for the aqueous polymerisation of methacrylic acid which is known to cause hydrolysis of CoBF[16].

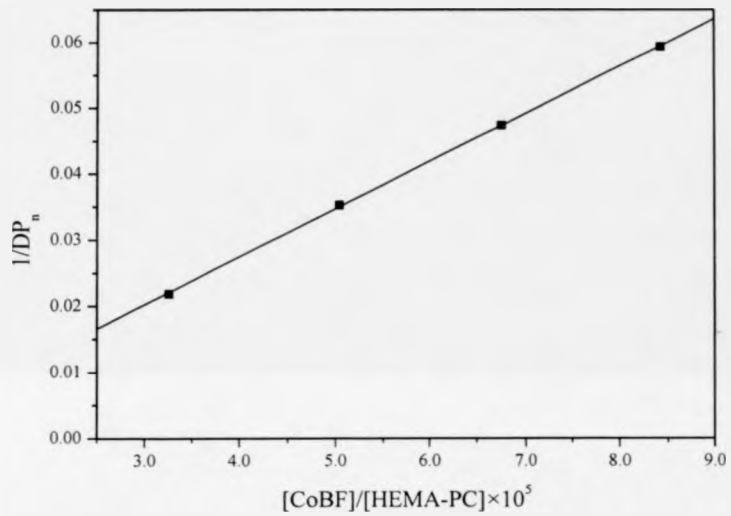

Figure 5.5, Pseudo *Mayo-plot* for the polymerisation of 2-(methacryloxyethyl)-2'-(trimethylammoniumethyl)phosphate in water/methanol at 80 °C in the presence of CoBF; apparent *Cs* = 725.

The ^{1}H NMR spectrum of a poly(HEMA-PC) macromonomer is shown in *figure 5.7*. The resonances at 5.89-6.00 ppm and 5.27-5.33 ppm are those of the vinyl protons of the macromonomer and residual monomer at 5.78-5.84 ppm and 5.33-5.40 ppm. This confirms the activity of the CoBF to produce macromonomer although it is suspected it is being deactivated throughout the reaction.

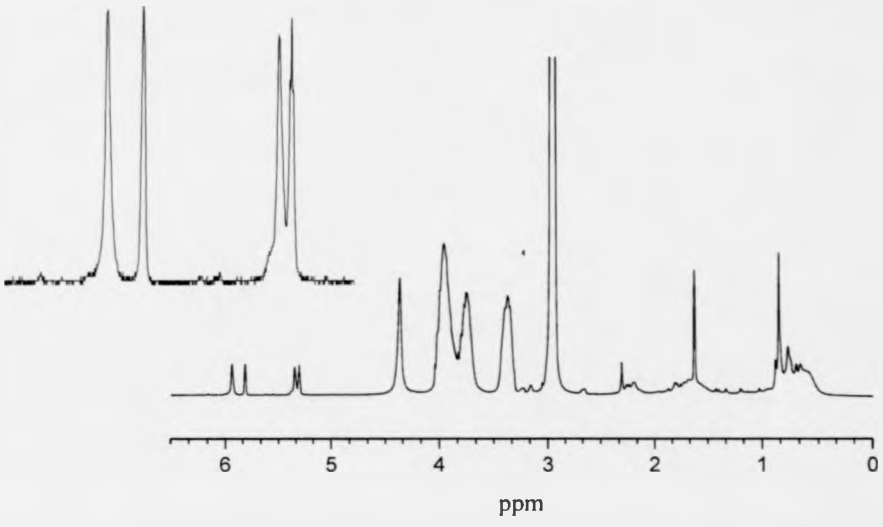

Figure 5.6, ^{1}H NMR in $CDCl_3/CD_3OD$ (70:30) of poly(2-(methacryloxyethyl)-2'-(trimethylammoniumethyl)phosphate macromonomer (*Mn* 1500) prepared in the presence of CoBF. Macromonomer vinyl proton resonances at 5.89-6.00 ppm and 5.27-5.33 ppm are shown in the insert

5.2.1.2 Statistical Copolymers

TRIS has a high affinity for oxygen and as such is useful as an additive in contact lenses to increase oxygen permeability. However, the monomer is extremely hydrophobic by copolymerising with HEMA-PC, a highly hydrophilic monomer, it is hoped that the resultant copolymer will be more soluble in hydrophilic media. These polymerisations were carried out as outlined for the homopolymerisations of HEMA-PC except ethanol was used in place of a water/methanol mixture at a temperature of 75 °C. Two reactions were carried out containing 20 and 40 % HEMA-PC, 150 ppm of CoBF was added to both reactions to dramatically limit molecular weight. Conversions, composition and molecular weight information was

obtained through ^{1}H NMR analysis. Molecular weight data were also obtained from SEC against PMMA standards using *Mark-Houwink* constants appropriate to MMA, *table 5.3*. Again we see that the polymerisations reach high conversion after just 6 hours and copolymers with molecular weights in the region predicted are produced. As would be expected with polymerisations that reach such high conversions the copolymers composition is the same as that of the feed. From SEC the copolymer containing 80 % TRIS had an *Mn* of 2200 and PDI of 1.75, typical for free radical chain transfer polymerisation. The copolymer containing 60 % TRIS had an *Mn* of 1600 and PDI of 1.17 this is low due to the high level of catalyst employed. However, the SEC data is not necessarily reliable but comparing with molecular weights obtained through ^{1}H NMR analysis show that they correlate relatively well.

Table 5.3, Reaction Conditions and Molecular Weight/Conversion Data for Copolymerisation of TRIS/HEMA-PC in Ethanol at 75 °C in the Presence of CoBF

	CVA (wt %)	% TRIS in copolymer	[CoBF]/ [Monomer] × 10^6	*Mn* (NMR)	*Mn* (SEC)	% Conv.
C1	12.2	79	149	2360	2200	93.4
C2	12.2	58	150	2010	1600	92.9

5.2.2 Conclusions

This novel feed method of cobalt mediated CCTP proves to be an invaluable synthetic route to water soluble macromonomers. In particular this method is beneficial for methacrylate monomers with functionality that usually prevents the use of controlled polymerisation methodologies without the need for protecting group chemistry. Aside

from these benefits low molecular weight polymers can be produced in very high yield in less time than through standard CCTP.

5.3 Transition Metal Mediated - Living Radical Polymerisation

Since the advent of TMM-LRP, papers covering a wide range of topics have appeared. Due to the mechanism by which TMM-LRP functions and the facile synthesis of appropriate alkyl halide initiators, the polymerisation technique is ideal for the formation of both polymers with α-terminal functionality and novel architecture. Indeed this aspect of the technique has been receiving increased interest in both academia and industry over the past year. A wide range of functional initiators have been reported including but by no means limited to hydroxyl, carboxylic acid, cholesterol, glycidyl and allyl functional alkyl bromides and chlorides[20-23]. From which α-terminal functional polymers with narrow molecular weight distributions and predefined molecular weights have been produced with no detrimental effects to the polymerisation. TMM-LRP has also been shown to be tolerant to a wide range of functional groups with polymerisations even having been carried out in ethylene carbonate, methanol, acetonitrile and pyridine with little or no detrimental effects[24]. This tolerance has led to the application of TMM-LRP to many different functional monomers including, 2-hydroxyethyl acrylate[25] glycidyl acrylate[26] acrylonitrile[27] and 2-(dimethylamino)ethyl methacrylate[28]. More recently both Armes[29-31] and Matyjaszewski[32] have reported TMM-LRP in aqueous solution using the Cu(I) bipy catalyst. The first two reports describe polymerisations of 2-hydroxyethylmethacrylate[32] and sodium methacrylate[29] at 90 °C using water-soluble initiators, the resultant polymers having relatively narrow polydispersity

indexes (PDI > 1.3). Subsequent publications from Armes have shown that both oligo(ethylene oxide) methacrylate (OEGMA) and sodium 4-vinylbenzoate can be polymerised by TMM-LRP at 20 °C. The polymerisations lasted between just 25-30 minutes and reached very high conversions (>90 %) in this time. The kinetic plots of these reactions were linear and the products had narrow polydispersity indexes (PDI ~1.2) indicating the polymerisations were living. The untold flexibility and obvious potential of TMM-LRP to the production of 'novel' polymers is the reason that the application of this technique to the polymerisation of HEMA-PC is investigated here.

5.3.1 Results and Discussion

Due to the solubility of poly(HEMA-PC) suitable solvents are limited to either water or alcohols. Conventional polymerisation techniques were used and different ratios of Cu catalyst, monomer and initiator were examined. Initially the use of copper(I) *N*-alkyl-2-pyridylmethanime complexes as catalysts were examined in both methanol and ethanol however, no polymerisation occurred even after 48 hours at 90 °C. This was also observed when the reactions were repeated using a Cu(I) 2,2'-bipyridine (bpy) complex. Matyjaszewski has previously shown that methanol has little detrimental effect on TMM-LRP using a Cu(I)bpy complex, therefore it is believed that the presence of alcohol is not responsible for the lack of polymerisation[24,33]. As discussed previously in this chapter (*section 5.2.1.1*) phosphoryl compounds are known to co-ordinate to copper via this group and so the presence of HEMA-PC may be preventing the formation of the active Cu catalyst.

Polymerisations of HEMA-PC carried out in water were more successful. A difunctional polyethylene glycol initiator (*Mn* 1100) was synthesised by reacting

poly(ethylene glycol) with 2-bromoisobutryl bromide using a modified method of that reported by Jankova[34]. The first set of polymerisations were carried out using *N*-*n*-propyl-2-pyridylmethanime (*n*-Pr) ligand. Armes[29] comments that these maybe hydrolyticly unstable, however within our research group studies have shown that no hydrolysis is observed when the complex is left in water or methanol for over 30 days. The polymerisations were carried out in D_2O (86 wt %) with ratios of [Cu(I)Br] : [Ligand] (*Lig*): [Initiator groups] (*Init*): [HEMA-PC] of 1:2:1:17 and 1:2:1:34 (theoretical *Mn*'s of 5000 and 10000) at 25 °C and conversions were determined through ^{1}H NMR analysis. It was found that in both cases over 95 % conversion was reached in ~5 minutes suggesting that the polymerisations were uncontrolled, most probably due to lack of deactivation. In a second set of polymerisations, bpy was used as the ligand instead of *N*-*n*-propyl-2-pyridylmethanime. Two identical polymerisations were conducted at 60 & 90 °C. The polymerisations were carried out in D_2O (86 wt %) with ratios of [Cu(I)Br] : [*Lig*] : [*Init*]: [HEMA-PC] of 1:2:1:17 (theoretical *Mn* of 5000) and conversions were determined through ^{1}H NMR analysis. Due to the nature of these polymers, it is not possible to obtain molecular weight information via SEC and *Mn* calculated through ^{1}H NMR analysis would just give the theoretical *Mn*. The reaction conditions for these polymerisations are outlined in *table 5.4* and the rate plots for the reactions with bpy shown in *figure 5.7*.

Table 5.4. Reaction conditions for TMM-LRP of HEMA-PC

	Lig	[HEMA-PC]/ [*Init*]	Temperature (°C)	Time (mins)	Conv. (%)	*Mn* (theory)
D1	*n-Pr*	17	25	5.0	97.6	4900
D2	*n-Pr*	34	25	6.5	96.2	9660
D3	*bpy*	17	60	120	90.2	4510
D4	*bpy*	17	90	38	90.2	4510

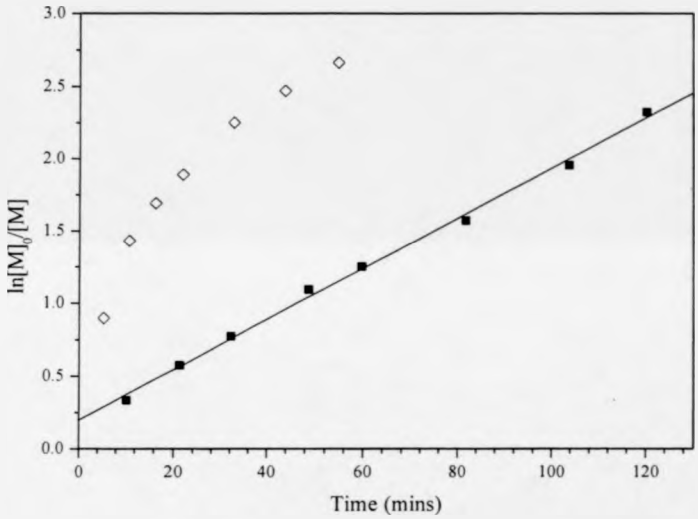

Figure 5.7 Rate plots for TMM-LRP of HEMA-PC (86 wt % D_2O, [CuBr]:[bpy]:[init]:[HEMA-PC], 1:2:1:17 D3 ■ at 60 °C and D4 ◇ at 90 °C)

For reaction D3 (60 °C) 90.2% conversion is reached after just 2 hours and as would be expected reaction D4 (90 °C) is even faster and after just 38 mins the polymerisation has reached 90.2 % conversion. The rate plot for reaction D3 is linear indicating that the radical concentration is constant throughout the reaction even at high conversion. However, the plot does not intercept the origin suggesting that there was an initial period of termination. This is not surprising given the high

concentration of initiator and catalyst with respect to monomer and is consistent with the persistent radical effect. At the higher temperature of 90 °C the reaction is considerably faster and the rate plot shows that the radical concentration decreases throughout the course of the reaction indicating that termination is occurring and that the polymerisation is uncontrolled.

5.3.2 Conclusions

Given that the rate plot at 60 °C is linear it can be concluded that TMM-LRP of HEMA-PC in aqueous solution is a viable method for production of poly(HEMA-PC) with predefined molecular weight. Whilst no molecular weight data is available for these polymers, given that previous studies have shown that aqueous solution TMM-LRP produces polymers with narrow molecular weight distributions there is no reason to suspect that these polymers are anything other than narrow.

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Chapter 6

Synthesis of Ultra Violet Blocking Polymers

6 Synthesis of Ultra Violet Blocking Polymers

Over the past decade society has become more conscious of the detrimental effects associated with exposure to the sunlight, in particular UV radiation, to both the skin and eyes. This has created a greater demand for products that protect against UV radiation and this extends to the contact lens market.

UV radiation can be divided into three wave bands labelled UVA (315 to 400 nm), UVB (280 to 315 nm) and UVC (100 to 280 nm)[1]. The majority of UVC radiation is absorbed by the atmosphere and poses little concern. However, exposure to UVA and UVB radiation, which are only partially absorbed by the atmosphere, offer potential harm. The cornea and conjuctiva absorb UVB radiation with some penetration to the anterior lens surface, see *section 2.1*, *figure 2.1* for a diagram of the eye. Over exposure can cause inflammation of the cornea and conjunctiva (snow-blindness) whilst long term exposure contributes to the formation of several ocular pathologies of the cornea (formation of cysts), conjuctiva (excessive tissue growth), lens (cataracts) together with retinal damage, many of which if left untreated can lead to permanent blindness[2,3]. The majority of UVA radiation is absorbed by the lens thus protecting the retina and there is some concern that UVA radiation is associated to occular conditions such as cystoid macular oedema (swelling and cysts on the surface of the retina)[3]. On a more clinical level UVA radiation is also a consideration for people who are aphakic (lacking a lens) are taking photosensitising medications[4] or have old intraocular lenses and thus lack the protective barrier provided by the lens. In these cases it is often necessary that absorbency of protective eye wear extends up to 400 nm[3].

Contact lenses are ideal for protection from UV radiation as they are situated on the surface of the eye and therefore prevent the "leakage" around the sides of the lens associated with sunglasses[5]. Of the different types of lenses available only soft contact lenses offer complete protection to the eye because they are the only lens to offer complete coverage of the cornea. For patients with conditions that require protection from UV radiation, contact lenses offer an advantage over sunglasses in terms of colour perception, optical clarity in low ambient light and cosmetic acceptability in winter and on overcast days[5]. As we have seen in *chapter 2* the main component of contact lenses are based around acrylic polymers. Studies have shown that UV/VIS absorption spectra are usually similar to PMMA indicating that the majority of standard contact lenses are transparent at the crucial range of the UV radiation spectrum. Therefore additives are needed to introduce the required absorption[2].

Another important consideration is photodegradation of the lens material. It is well known that PMMA has excellent UV stability yet degradation of the ester groups to form migrating and polymer bound free radicals still occurs. This photodegradation, which results in material weakening and discolouration, can be prevented by employing photostabilisers[6]. Analogous processes are anticipated in acrylate lens materials however, due to much shorter exposure times than typical PMMA products (*e g.* Perspex©) there is a lower tendency to photodegradation.

There are a number of effective commercially available UV absorbers, many of which are phenol based, that absorb to differing degrees in different areas of the UV spectrum dissipating the energy absorbed harmlessly[7]. Currently the two main types of UV blockers used in contact lenses are based on either the benzophenone or the benzotriazole families[5]. The most notable of all UV absorbers are based upon 2(2-hydroxyphenyl)-2H-benzotriazole, *figure 6.1*.

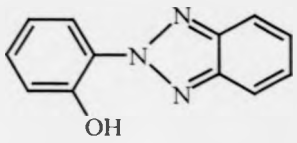

Figure 6.1, Structure of 2-(2'-hydroxyphenyl)-2*H*-benzotriazole

Typically this family of compounds absorb from 260 to 380+ nm with a sharp cut off just before the range of the visible spectrum, this region coincides with that of the UVA and UVB radiation range (the benzophenone compounds have a cut off of 360 nm). Halogenation of the benzotriazole group has been shown to extend the range of coverage up to and beyond 400 nm making this family of molecules ideal[5,8]. Not only are the 2(2-hydroxyphenyl)-2*H*-benzotriazole's exceptionally good UV absorbers but they are also among the most effective of UV stabilisers known[8].

Contact lenses must be free from extractable molecules (such as residues of polymerisation) that might cause inflammation of the eye and the surrounding tissue. Therefore it is not plausible to simply add these small molecules to the lens formulation which would result in the blocker being leached by tears. Incorporation of functionality into the UV absorber, which will bond covalently into the polymer network, has proven to be a simple and effective way of overcoming this. For methacrylic based lenses this involves the incorporation of a vinyl group so that the blocker can be copolymerised into the lens material. The addition of these materials to a lens must have a minimal effect upon mechanical properties and, in the case of soft contact lenses, equilibrium water content so as not to deteriorate other important properties of the lens.

A number of copolymers containing UV radiation absorbers are commercially available for contact lens producers. These include copolymers of

2-benzophenoneethyl methacrylate with 2-hydroxyethyl methacrylate (HEMA), vinylpyrrolidone, α-methylstyrene and ethylene glycol dimethacrylate proposed for use in soft[9] or hard contact lenses[9] or intraocular lenses[9]. Copolymers of various benzotriazole methacrylates with MMA, α-methylstyrene or methacrylic acid have also been recommended for use in contact lenses[9-11].

In order to maintain a competitive edge Biocompatibles wish to produce their own UV radiation absorbing material for use in their Proclear® range of soft contact lenses. An examination of the patent literature has lead to the elimination of many benzotriazole monomers as viable options for use in contact lenses. However, two commercially available monomers not yet fully covered in the patent literature are 2-(2'hydroxy-5'methacryloxyethyl-phenyl)-2*H*-benzotriazole (NORBLOC) and 2-(2'hydroxy-3-*t*-butyl-5-vinyl phenyl)-5-chloro-2*H*-benzotriazole (UVAM). *figure 6.2.*

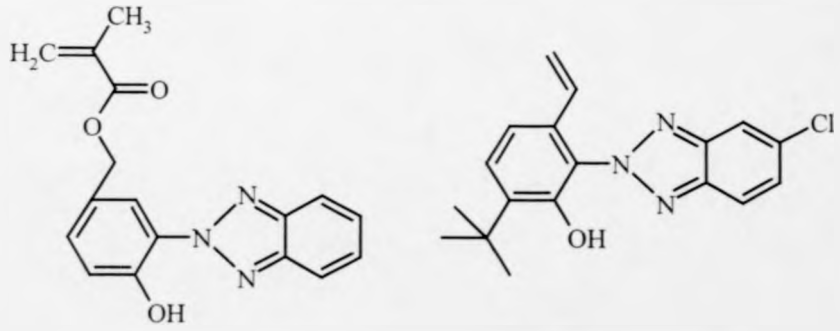

Figure 6.2. Structures of 2-(2'hydroxy-5'methacryloxyethyl-phenyl)-2*H*-benzotriazole (NORBLOC) and 2-(2'hydroxy-3-*t*-butyl-5-vinyl phenyl)-5-chloro-2*H*-benzotriazole (UVAM)

NORBLOC absorbs up to 380 nm whilst UVAM covers a more complete range up to 410 nm due to the presence of the chlorine substituent on the benzotriazole group however, this extends into the visible spectra giving the monomer a bright yellow colour. The amount of energy absorbed by a sample is a function of thickness, typically somewhere between 0.5 to 5 weight percent of the polymer needs to be UV blocker to sufficiently reduce transmitance through a thin film such as a contact lens[2]. Biocompatibles have established that for their range of lenses to have an UV absorbing level equivalent to that of their closest competitors range of contact lenses, Johnson and Johnson's Acuvue, then only 0.2-0.6 wt % of either NORBLOC or UVAM are required. The high colour of UVAM is therefore not likely to be a problem and a small amount of colouring would be acceptable.

It has been found that neither NORBLOC nor UVAM can be added directly to the contact lens formulation due to poor solubility particularly in hydrophilic media. This is of concern on several levels when considering the design of a soft (or hydrophilic) contact lens. Primarily their lack of solubility typically leads to lenses that are phase separated therefore lacking optical clarity. Another consideration is that the effectiveness of a UV radiation blocker is limited by its solubility or compatibility in its environment[12]. Interestingly Sustic *et al.* examined the UV absorption of a number of 2(2-hydroxyphenyl)-2*H*-benzotriazoles and found that generally when dissolved in more polar solvents a broader UV absorption spectrum was observed[8]. A similar study revealed that when 2(2-hydroxyphenyl)-2*H*-benzotriazoles are incorporated into a polymer structure the general characteristics of the UV spectrum were found to be determined by the "next neighbour" in the macromolecule and not by the solvent[8,13].

In order to overcome the problems associated with solubility and compatibility there are two options. The first is the use of a coating, however there are many associated

drawbacks such as non-permanency, reduced absorbency due to coating thickness, and the addition of a processing step. More importantly the coating will undoubtedly affect the interaction of the lens with the eye's phospholipid layer reducing wettability of the lens and ultimately causing irritation. An alternative option is the production of copolymers of an UV blocking monomer with a more hydrophilic monomer such as HEMA that contain a polymerisable functional group. The presence of this functional group allows the materials to be copolymerised to form a lens. It is preferential that these copolymers have a low molecular mass as only low levels of the materials would be required and it is important that the material is well distributed throughout the lens.

As we have already seen in previous chapters catalytic chain transfer polymerisation is ideally suited to this task. The *Cs*'s for both NORBLOC (Cs ≈ 4100) and UVAM (Cs ≈ 200) with CoBF have been calculated and random copolymers of the two UV blocking materials with both MMA and HEMA have been prepared. The activity of the NORBLOC macromonomers as chain transfer agents has been examined by their copolymerisation with TRIS. Block copolymers of NORBLOC with both TRIS and HEMA have also been prepared.

6.1 Homopolymerisations of NORBLOC

6.1.1 Results and Discussion

To test the effect of the NORBLOC functionality on CCTP a series of polymerisations were carried out from which the *Cs* for the system was calculated. Reactions were carried out as described in *section 7.2.5*, for determination of chain

transfer constants. A series of five polymerisations was carried out containing four different levels of CoBF and one, as a control, in the absence of catalyst. Polymerisations were carried out in 88 wt % toluene with 0.2 wt % dimethyl-2,2'-azobis-isobutyrate (V-601 initiator) at 60 °C for 55 minutes. Such a high dilution was required due to the poor solubility of the monomer in the chosen and other appropriate solvents. Molecular weight information was obtained from SEC calibrated with PMMA using *Mark-Houwink* parameters appropriate to PMMA in THF at room temperature. A summary of the reaction conditions and molecular weight information of the resultant polymers are contained in *table 6.1*. Conversions have been estimated from SEC and NMR analysis to be less than 10 %. As the ratio of catalyst to monomer increases a steady decrease in molecular weight is observed. With as little as 0.42 ppm of CoBF an *Mn* of 84000 was recorded, some 66000 less than the *Mn* (150000) of the polymer from the control reaction containing no catalyst. There is no significant difference in the polydispersity index of the polymers, however at ~1.6 the values are low for chain transfer polymerisation of a methacrylate.

Table 6.1. Reaction Conditions and Molecular Weight Data for Polymerisation of NORBLOC in Toluene at 60 °C in the Presence of CoBF

	[CoBF]/ [M] $\times 10^7$	*Mn*	DP_n	$1/DP_n \times 10^3$	*Mw*	DP_w	$2/DP_w \times 10^3$	PDI
A1	0	150000	470	2.148	235000	730	2.740	1.57
A2	1.06	126000	390	2.566	192000	600	3.357	1.53
A3	1.55	116000	360	2.786	179000	550	3.613	1.54
A4	3.18	91400	280	3.535	146000	450	4.416	1.60
A5	4.24	84000	260	3.846	135000	420	4.780	1.61

Figure 6.3 shows the *Mayo-plots* of $1/DP_n$ and $2/DP_w$ vs. the ratio of catalyst to monomer. From the gradient of the line of best fit we obtain a value for the chain transfer constant (*Cs*). For a detailed discussion of methods to calculate the *Cs* see *section 1.4.2.1*. *Cs* values of 4110 ± 210 and 4810 ± 250 have been calculated from *Mayo-plots* DP_n and $2/DP_w$ respectively. These values are particularly low for a catalytic chain transfer agent such as CoBF with a methacrylate monomer. Co-ordinating solvents such as methanol have been shown to cause a reduction in the *Cs* due to competition between monomer, polymer and the solvent at the Co centre effectively reducing the level of active catalyst[14]. Whilst toluene is not known to co-ordinate reports have also found that toluene decreases catalyst activity and whilst no conclusions have been drawn the most probable explanation is the presence of some impurity not removed through standard distillation[15]. Therefore the most probable cause for the low observed *Cs* value is the high level (88 wt %) of toluene used in the polymerisations. It is also possible that the monomer itself co-ordinates via the three nitrogen atoms present.

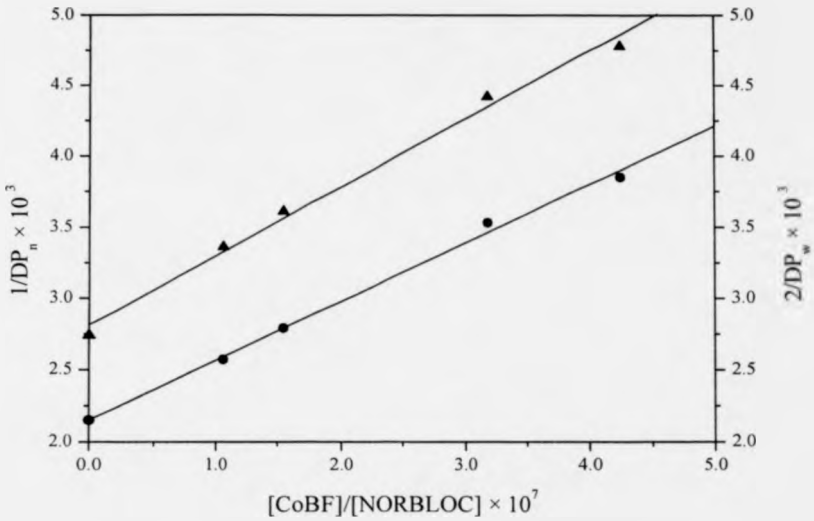

Figure 6.3, Plot of $1/DP_n$ (▲) and $2/DP_w$ (●) vs. [CoBF]/[NORBLOC] for the polymerisation of NORBLOC in toluene at 60 °C in the presence of CoBF. Chain transfer constants calculated at 4110 and 4810 respectively

Using the data obtained from the *Mayo-plot* a series of low molecular weight NORBLOC macromonomers were prepared. Reactions were prepared using standard polymerisation methodology and were carried out in 88 wt % toluene at 60 °C for 48 hours with 0.2 wt % V601 initiator, after 24 hours an additional 0.1 wt % of initiator was added. The polymers were purified by precipitation from acetone and subsequently dried in vacuum at 40 °C for 48 hours. Molecular weight and conversion data were calculated from ^{1}H NMR analysis and size exclusion chromatography. Catalyst concentrations and theoretical and experimental molecular weight information is listed below, *table 6.2*.

Table 6.2, Molecular Weight and Conversion Data for the Polymerisation of NORBLOC at 60 °C in Toluene in the Presence of CoBF

	[CoBF]/[M] $\times 10^6$	Mn_{theo} $1/DP_n$	Mn_{theo} $2/DP_w$	*Mn* (SEC)	PDI	*Mn* (NMR)	% Conversion
B1	10.4	7600	4000	3400	1.86	4400	98.6
B2	20.8	3800	3200	2300	1.88	3400	98.6
B3	31.2	2500	2200	1600	1.92	2500	99.0

Due to the inaccuracy associated with SEC when analyte and calibrant polymers differ, the molecular weight information obtained by NMR is considered to be more accurate. However, SEC provides information concerning molecular weight distributions otherwise unobtainable. The polydispersity index of these polymers is higher than for those of the polymers from the *Cs* determination (*table 6.1*). This can be explained by the increase in the ratio of catalyst to monomer as the reaction proceeds to higher conversion. Thus the average molecular weight of polymers formed will reduce through the course of the reaction increasing the overall molecular weight distribution of the polymers. Comparing the theoretical *Mn* of the polymers predicted from the *Mayo-plots* with the experimental data shows that there is good correlation even at the low molecular weight range. However, the theoretical *Mn* of 7600 obtained from the *Mayo-plot* ($1/DP_n$) for reaction B1 is higher than the experimental value obtained. The theoretical values from the $2/DP_w$ plot correlate extremely well with the molecular weights calculated from NMR analysis. The ^1H NMR spectra of a NORBLOC© macromonomer is shown in *figure 6.4*. The resonances of the vinyl protons of the macromonomer are found at 6.02-6.26 ppm and 5.27-5.51 ppm.

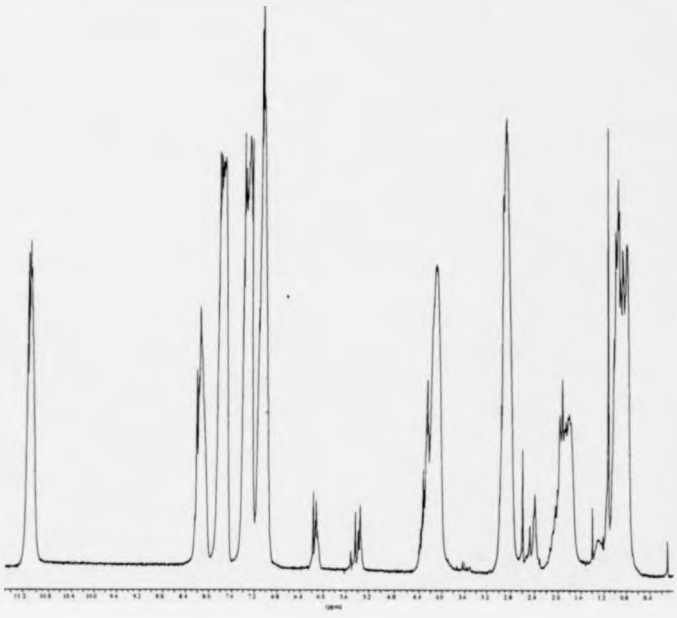

Figure 6.4, ^{1}H NMR in $CDCl_3$ of NORBLOC macromonomer (*Mn* 2500) prepared in the presence of CoBF. Macromonomer vinyl proton resonances at 6.02-6.26 ppm and 5.27-5.51 ppm

6.2 Synthesis of Statistical Copolymers Containing NORBLOC

6.2.1 Results and Discussion

It was anticipated that copolymers of NORBLOC with a hydrophilic monomer such as HEMA will increase solubility in hydrophilic media. NORBLOC has been shown to have no adverse affect on CCTP other than a lowering in the observed *Cs*. Therefore a series of MMA / NORBLOC (79:21) statistical copolymers were prepared. MMA was used initially as it has been the focus of many studies and

therefore its behaviour in this system is well documented. This also gives the advantage of providing an estimate for the level of catalyst required for subsequent polymerisations with other methacrylate monomers. The series of copolymerisations of MMA / NORBLOC (79:21) contained various levels of CoBF to produce macromonomers of different molecular weights. For the homopolymerisation of MMA in toluene in the presence of CoBF a *Cs* of 20000 has been reported[15]. Considering the high volumes of solvent and the presence of NORBLOC the expected Cs for this system would be less than 20000. Therefore the level of catalyst used in these experiments was adjusted accordingly so that macromonomers produced should have molecular weights in the region of 1-5,000. The reactions were prepared using standard polymerisation methodology and carried out in 86 wt % toluene at 65 °C for 48 hours with 0.23 wt % AIBN. The polymers were isolated by rotary evaporation of solvent and subsequently placed under high vacuum for 24 hours (2.5×10^{-2} mbar). Molecular weight and conversion data were calculated from ^{1}H NMR analysis and size exclusion chromatography. Catalyst concentrations and molecular weight information are listed below, *table 6.3*.

Table 6.3, Reaction Conditions and Molecular Weight Data for Copolymerisation of MMA/NORBLOC (79:21) in Toluene at 65 °C in the Presence of CoBF

	[CoBF]/ [M] × 10^6	% NORBLOC in Copolymer	*Mn* (SEC)	PDI	*Mn* (NMR)	Conversion (%)
C1	0	20.2	30974	2.75	-	99
C2	3.33	26	1100	2.27	1500	97
C3	6.72	22	1200	2.00	1100	98
C4	13.26	23	900	1.64	1000	95

The *Cs* for this system is assumed to be 20000 giving predicted molecular weights for reactions C2, C3 and C4 of 1500, 750 and 400 respectively. A comparison between these theoretical molecular weights and those observed shows this difference to be negligible. One explanation is that the apparent *Cs* for the copolymerisation system is dependent upon the ratio of MMA radicals to NORBLOC radicals. If a higher number of MMA radicals are present at the beginning of the polymerisation then the *Cs* will be nearer to that of MMA. As conversion increases the concentration of MMA radicals would decrease and the *Cs* would begin to approach that of NORBLOC. This variation in *Cs* throughout the polymerisation would be in line with the unusual trend in polydispersity observed. Ideally determination of reactivity ratios and partial monomer conversion data would be required to provide a more thorough analysis. It is also noted that the molecular weight of the control is considerably lower than for the homopolymerisation of MMA, which under similar conditions would be expected to be nearer 100000. Alternatively as the *Cs* for MMA is significantly higher than for NORBLOC chain transfer reactions will be dominated by MMA. SEC analysis of the polymers with both differential refractive index and UV detectors showed that they all contained a strong chromophore at 254 nm throughout the polymer distribution. From this it can be concluded that NORBLOC is present throughout the mass distribution and therefore the polymers are true random copolymers and not a blend of two homopolymers.

Having demonstrated the applicability of CCTP to the production of low molecular weight methacrylate copolymers containing NORBLOC a similar series of HEMA / NORBLOC (80:20) macromonomers were prepared. This series of random copolymerisations contained levels of CoBF predicted to produce macromonomers with molecular weights below 5000. This is required for molecular weight analysis to

be possible. The reactions were prepared using standard polymerisation methodology and were carried out in 88 wt % acetone / methanol (95:5) at 55 °C for 48 hours with 0.22 wt % AIBN. The polymers were isolated by rotary evaporation of solvent and subsequently placed under high vacuum for 24 hours (3×10^{-2} mbar). Molecular weight and conversion data were calculated from ^{1}H NMR analysis and size exclusion chromatography. Catalyst concentrations and molecular weight information are listed below, *table 6.4*.

Table 6.4, Reaction Conditions and Molecular Weight Data for Copolymerisation of HEMA/NORBLOC (80:20) in Acetone/Methanol (5 %) at 55 °C in the Presence of CoBF

	[CoBF]/ [M] $\times 10^{6}$	% NORBLOC in Copolymer	*Mn* (SEC)	PDI	*Mn* (NMR)	Conversion (%)
D1	1.43	18.9	2600	1.51	2300	80.3
D2	1.76	19.3	2300	1.50	2000	75.7
D3	4.18	18.16	2000	1.44	1400	70.8

From the above table it can be seen that with as little as 1.43 ppm of CoBF very low molecular weight oligomers are produced. Confirming the applicability of CCTP to the production of Biocompatibles desired products. Whilst several parameters differ (temperature and solvent) it was presumed that the *Cs* for this system would be similar to that of the MMA / NORBLOC polymerisations previously described (around 20000). If this were so then at the levels of catalyst used D1, D2 and D3 would have molecular weights in the region of 6000, 4700 and 2000 respectively. This is not observed and a *Cs* nearer approximately 35000 is estimated from the calculated molecular weights. This is surprising as this value is approaching the *Cs* of 40000 calculated for MMA in bulk at 60 °C by Haddleton *et al.*[14]. The low

polydispersity of the samples is explained by the production of monomer during the catalytic cycle. Again SEC analysis showed that they all contained a strong absorption at 254 nm throughout the polymer distribution. From this it can be concluded that NORBLOC is present throughout the mass distribution and that the polymers are random copolymers and not a blend of two homopolymers.

6.3 Synthesis of Block Copolymers Containing NORBLOC

6.3.1 Results and Discussion

The use of macromonomers prepared by CCTP to produce block copolymers containing NORBLOC was investigated. The use of macromonomers as chain transfer agents and their use in the production of both block and graft copolymers is discussed in *section 1.5.4*, although, it is important to note that the block copolymer products of these reactions contain a vinyl functional end group. For the materials to be of use in the formulation of contact lenses they must be of sufficiently low molecular weight so that they contain a high proportion of vinyl groups. Blocks are of interest as an alternative to the random copolymers already discussed and will undoubtedly offer different physical properties. To test the reactivity of the NORBLOC macromonomers prepared in *section 6.1*, a series of polymerisations of TRIS were carried out in which the concentration of macromonomer was varied. The macromonomer studied was example B3 that had a molecular weight of 2500, as determined by ^{1}H NMR analysis. The reactions were prepared using standard polymerisation methodology. The levels of solvent, initiator and macromonomer used in this series of polymerisations are tabulated below, *table 6.5*. The reactions were

heated to 65 °C for 48 hours and the products isolated by removal of volatiles in vacuo, *table 6.6*.

Table 6.5, Reaction Conditions for Polymerisation of TRIS in the Presence of NORBLOC Macromonomer in Toluene at 65 °C

	TRIS (mL)	B3 (g)	B3 (Mol %)	NORBLOC % by unit	AIBN (wt %)	Toluene (wt %)
E1	2.0	0	0	0	0.22	80
E2	5.0	1.17	4	25	0.25	83.4
E3	3.0	2.16	12	50	0.28	87.4
E4	1.25	2.61	28	75	0.33	91.3

Table 6.6, Molecular Weight and Composition Data for Polymerisation of TRIS in the Presence of NORBLOC Macromonomer in Toluene at 65 °C

	% TRIS in Copolymer	*Mn* (SEC)	*Mw* (SEC)	PDI	Conversion (%)
E1	100	287000	523000	1.82	96.4
E2	-	2600	56400	21.51	87.6
E3	-	1800	8900	5.03	89.9
E4	-	1600	4600	2.87	21.2

Whilst the molecular weight of the products appears to have decreased as the level of macromonomer present increases the SEC chromatograms show the samples to be bimodal and hence the large polydispersity indices observed. SEC using an UV detector measuring absorbency at 254 nm showed that the products of these reactions only absorb in an identical position to the original NORBLOC macromonomer. This suggests that the products of these reactions were homopolymers of TRIS. However, if we exclude the area of the SEC traces corresponding to the NORBLOC macromonomer from the analysis the molecular weights of the TRIS polymers

As would be expected the presence of the macromonomer has reduced the molecular weights of the products compared to the control. SEC using an UV detector measuring absorbency at 254 nm showed that the products of these reactions all absorb very strongly throughout the entire range of the polymer. *Figure 6.5* shows the DRI chromatogram of both the TRIS macromonomer and sample F2 along with the UV chromatogram for F2.

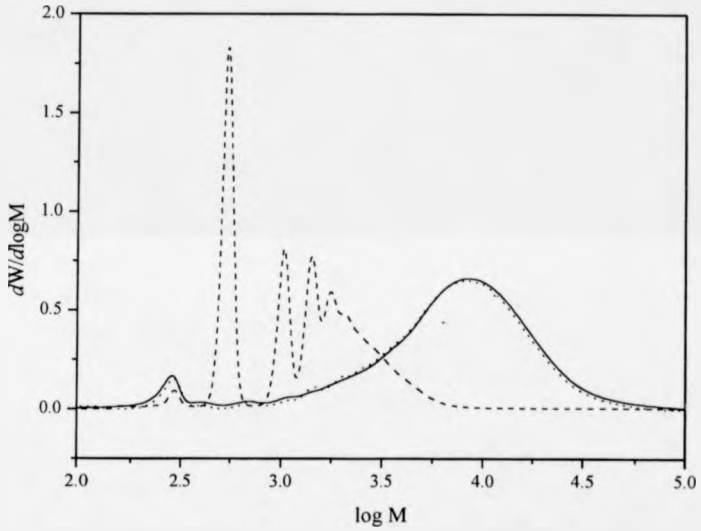

Figure 6.5, DRI and UV SEC chromatograms of both TRIS macromonomer (DRI ---) and polymer F2 (DRI ——, UV ·····)

The UV absorbence of this polymer extends throughout the mass envelope corresponding to the DRI trace. If TRIS macromonomer were present at any significant level there would be a decrease in the intensity of the UV chromatogram in the region the TRIS macromonomer elutes. Examination of the other two samples shows identical results. Having shown that the production of block copolymers containing NORBLOC is plausible by this method a HEMA macromonomer was prepared using CCTP as described in *section 7.2.3*. The macromonomer was found to

have a molecular weight of 2200 g.mol^{-1} from ^{1}H NMR analysis. Again a series of reactions were carried out in which the level of macromonomer was varied and the reactions were carried out as described for those involving the NORBLOC macromonomer, *table 6.9*. The reactions were heated to 55 °C for 48 hours and the products isolated by removal of volatiles in vacuo, *table 6.10*.

Table 6.9, Reaction Conditions for Polymerisation of NORBLOC in the Presence of HEMA Macromonomer in Acetone/Methanol (5 %) at 55 °C

	NORBLOC (g)	HEMA (g)	HEMA (Mol %)	HEMA % by unit	AIBN (wt %)	Solvent (wt %)
G1	3.0	0.0	0	0	0.22	90.0
G2	3.75	0.5	1.9	25	0.23	89.9
G3	2.5	1.0	5.5	50	0.22	90.0
G4	1.68	2.0	14.7	75	0.26	92.3

Table 6.10, Molecular Weight and Composition Data for Polymerisation of NORBLOC in the Presence of HEMA Macromonomer in Acetone/Methanol (5 %) at 55 °C

	% NORBLOC in Copolymer	*Mn* (SEC)	*Mw* (SEC)	PDI	Conversion (%)
G1	100	46200	120000	2.58	79.8
G2	67.4	29600	110800	3.74	94.2
G3	43.9	16000	45400	2.84	89.2
G4	20.2	3000	10800	3.61	80.7

The SEC DRI chromatograms of samples G2, G3and G4 are bimodal with the second peak corresponding to HEMA macromonomer. There is a slight decrease in molecular weight as macromonomer concentration is increased however, this is only significant at high concentrations (G4 – 15 mol % macromonomer).

Whilst this method of macromonomer production seems unsuccessful there are alternative methods of synthesis available. Alternative methods of block copolymer formation worth considering include transition metal mediated living radical polymeriation and radical addition fragmentation transfer polymerisation as discussed in *Chapter 1*.

6.4 Homopolymerisations of UVAM

6.4.1 Results and Discussion

A series of polymerisations was carried out so as to determine the chain transfer constant as described in *section 7.2.5*. Five polymerisations were carried out with four containing different levels of CoBF and one, as a control in the absence of catalyst. The polymerisations of UVAM were carried out in 89 wt % toluene with 0.2 wt % V601 at 60 °C for 15 minutes. A high dilution was required due to the poor solubility of the monomer in the chosen and other appropriate solvents. Molecular weight information was obtained from SEC calibrated with polystyrene using *Mark-Houwink* parameters appropriate to polystyrene in THF at room temperature, $K = 14.1 \times 10^{-5}$ dLg^{-1} and $\alpha = 0.70$. A summary of the reaction conditions and molecular weight information of the resultant polymers are contained in *table 6.11*. Conversions were estimated from SEC analysis as less than 5 %. As the ratio of catalyst to monomer increases a decrease in molecular weight is observed. To achieve significant reduction in molecular weight from the control a reasonably high quantity of CoBF is required with 39.2 ppm producing a polymer with *Mn* of ~33000. There is a slight decrease in

the polydispersity index of the CCTP reactions in comparison to the control, however no general trend is observed.

Table 6.11, Reaction Conditions and Molecular Weight Data for Polymerisation of UVAM in Toluene at 60 °C in the Presence of CoBF

	[CoBF]/ [M] $\times 10^6$	*Mn*	DP_n	$1/DP_n$ $\times 10^3$	*Mw*	DP_w	$2/DP_w$ $\times 10^3$	PDI
H1	0	129000	400	2.54	296000	900	2.21	2.30
H2	9.8	74900	210	4.37	135500	410	4.84	1.81
H3	19.6	58900	180	5.56	116100	350	5.65	1.97
H4	29.4	62000	190	5.28	111700	340	5.87	1.80
H5	39.2	32700	100	10.02	59000	180	11.11	1.80

Figure 6.6 shows the *Mayo-plots* for $1/DP_n$ and $2/DP_w$ vs. the ratio of catalyst to monomer. From the gradient of the line of best fit we obtain a value for the chain transfer constant (*Cs*). For a more detailed discussion of methods to calculate the *Cs* see *section 1.4.2.1. Cs* values of 190 ± 15 and 220 ± 25 have been calculated from the $1/DP_n$ and $2/DP_w$ plot respectively, which correlate well.

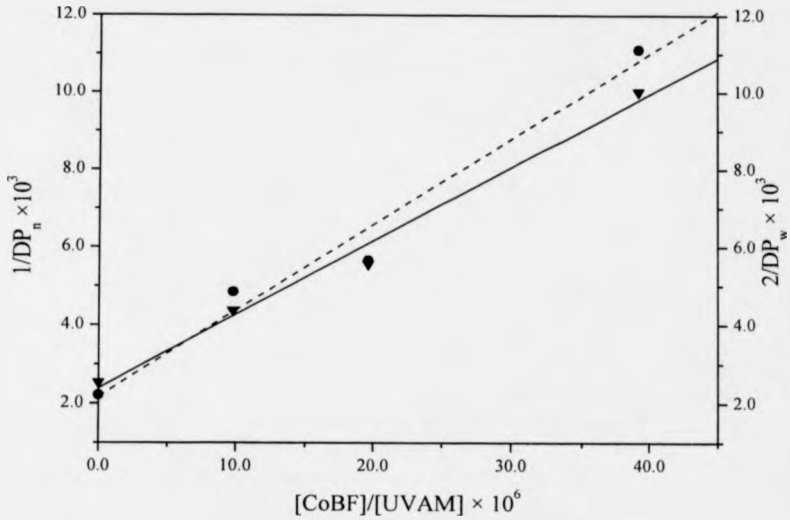

Figure 6.6, Plot of $1/DP_n$ (▼,——) and $2/DP_w$ (●, – – – –) vs. [CoBF]/[UVAM] for the polymerisation of UVAM in toluene at 60 °C in the presence of CoBF. Chain transfer constants calculated at 190 and 220 respectively

Polymerisation of styrene in bulk at 60 °C in the presence of CoBF a *Cs* of 1390 has been reported[15]. The much lower *Cs* of ~200 for the UVAM system is explained by the presence of toluene in the system as discussed in *section 6.1.1* and as with NORBLOC there is the possibility of monomer co-ordination via the three nitrogen atoms to the Co catalyst. The reason these values are significantly lower than values for methacrylates is explained in *section 1.5.2*.

6.5 Synthesis of Statistical Copolymers Containing UVAM

The aim is to produce low molecular weight macromonomers of HEMA containing approximately 20 % UVAM. Initially copolymers of MMA and UVAM were synthesised because more studies have focused on MMA than HEMA. This also gives

the advantage of providing an estimate for the level of catalyst required in the HEMA / UVAM polymerisations to target a specific molecular weight. For these polymers to be applicable to contact lens formulation they need to contain a terminal double bond. Due to the presence of the styrenic based UVAM, even if at low levels, a significant percentage of the polymers may have a UVAM terminus and thus an internal unsaturated bond.

6.5.1 Results and Discussion

6.5.1.1 Statistical Copolymerisation of MMA / UVAM

A series of MMA / UVAM (79:21) random copolymers were prepared using different levels of CoBF to produce macromonomers of different molecular weights. Reactions were carried out using standard polymerisation methodology in 88 wt % toluene at 60 °C for 24 hours with 0.18 wt % AIBN. The polymers were isolated by precipitation into hexane and removal of volatiles in vacuo, *table 6.12*. SEC with both DRI and UV detection analysis showed a uniform relationship between the two chromatograms confirming the incorporation of UVAM throughout the full distribution of the copolymers.

Table 6.12, Reaction Conditions and Molecular Weight Data for Copolymerisation of MMA / UVAM (79:21) in Toluene at 60 °C in the Presence of CoBF

	[CoBF]/ [M] $\times 10^6$	% UVAM in Copolymer	*Mn* (SEC)	PDI	*Mn* (NMR)	% Conversion
I1	0.00	35.2	48800	3.13	-	58.8
I2	5.96	35.3	9100	2.12	9500	58.6
I3	11.92	34.5	3800	2.02	4800	36.7
I4	17.88	35.3	2800	2.03	4600	32.5
I5	23.84	27.5	2500	2.13	5100	38.6

Greuel and Harwood have examined the CCT copolymerisation of MMA / styrene using a high level of a cobaloxime/pyridine complex[16]. The main products of their reactions were dimers of MMA, styrene and MMA/Styrene. They conclude that the relative amount of styrene end groups is proportional to the percentage of styrene in the feed. They also note that hydrogen atom donation from the Co(III)-H shows preference towards styrene. A more thorough kinetic investigation of the copolymerisation of styrene and MMA was carried out by Heuts *et al.* in which they noted that the average chain transfer constant is non-linear with the monomer feed composition. This can be explained by the fact that the fraction of radicals with a styrene terminal unit is higher than the fraction of styrene in the monomer feed[17]. From a *Mayo-plot* ($2/DP_w$) of the results listed in *table 6.12*, an apparent *Cs* of 1300 ± 100 was calculated for the copolymerisation of MMA with UVAM. Previously the *Cs* for MMA in toluene at 60 °C with CoBF has been calculated at 20000 and we have observed the *Cs* of UVAM as ~200[15]. The ratio of MMA to UVAM gives a predicted *Cs* value of ~16000 however, the apparent *Cs* measured is significantly less. The explanation put forward by Heuts *et al.* for their experiments with MMA/styrene explains this large difference. This theory predicts copolymers with a significantly

high proportion of UVAM compared to the feed, suggesting that a higher proportion of radicals would have a UVAM terminal unit than expected from the ratio of the monomer feed. From ^{1}H NMR analysis it should be possible to determine the relative ratio of styrenic to methacrylate end groups of at least the lower molecular weight polymers. There are four possible end groups for the polymerisation between UVAM and MMA resulting in the difference between the methacrylate and styrenic units, as shown for MMA and styrene in *figure 6.7*.

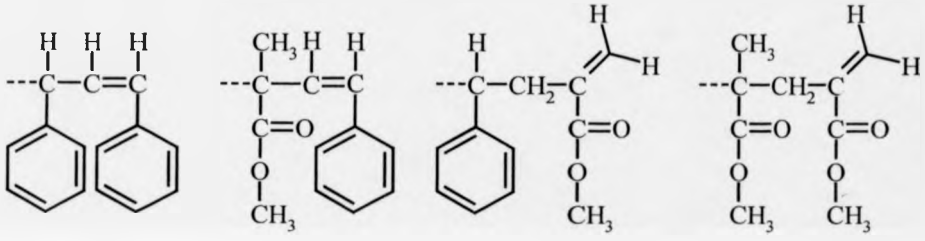

Figure 6.7, Four possible end groups from copolymerisation of styrene with MMA in the presence of a catalytic chain transfer agent

For the MMA/styrene dimers that Greuel and Harwood synthesised they showed that in the ^{1}H NMR three different vinylic end groups were detected[16]. The resonance of the protons on the internal double bond of the styrene terminal dimers were found at ~6.5 ppm whilst two sets of resonances were detected for the unsaturated methacrylate end group. Those at 5.6 and 6.3 ppm for the MMA-MMA dimer and 5.4 and 6.2 ppm for the Sty-MMA dimer. It would be predicted that a similar pattern would be observed for chains larger than dimer and also for the UVAM / MMA copolymers discussed here. The ^{1}H NMR spectra of samples E2 – E5 show only the vinyl protons of the methacrylate end group with broadening preventing further assignment. The resonance of any styrenic terminated macromonomers may be hidden under the resonance of the benzotriazole group at 6.6-7.1 ppm. The difference in the

molecular weights obtained from ^{1}H NMR and those by SEC is most probably explained by the exclusion of the styrenic terminal end groups in the ^{1}H NMR analysis. This would mean that molecular weights calculated by ^{1}H NMR would be higher than the actual molecular weight of the oligomers.

6.5.1.2 Statistical Copolymerisation of HEMA/UVAM

A second set of copolymerisations were carried out in which UVAM was polymerised with the hydrophilic monomer HEMA, in order to synthesise low molecular weight oligomers with a UVAM content of approximately 20 %. Reactions were carried out using standard polymerisation methodology in 88 wt % 2-butanone at 60 °C for 24 hours with 0.19 wt % AIBN. The polymers were precipitated from hexane and isolated by evaporation of volatiles in vacuo, *table 6.13*.

Table 6.13, Reaction Conditions and Molecular Weight Data for Copolymerisation of HEMA/UVAM (80:20) in 2-Butanone at 60 °C in the Presence of CoBF

	[CoBF]/ [M] x10^6	% UVAM in Copolymer	*Mn* (SEC)	PDI	% Conversion
J1	24	35	3300	1.60	33
J2	36	26	2100	1.48	22

The presence of CoBF results in the production of low molecular weight materials. The polydispersity of both materials are significantly low due to the quantity of monomer that will be produced by chain transfer reactions at these high catalyst concentrations. As monomer is not included in the SEC analysis this leads to a much lower observed molecular weight distribution than is typical of a free radical reaction. As observed in the polymerisations of MMA with UVAM these oligomers contain a

higher proportion of UVAM than the ratio of monomer in the feed. Therefore, we would expect to see some fraction of the macromonomers containing a styrenic terminus. As with the MMA / UVAM polymers there is an overlapping of resonances in the ^{1}H NMR and thus the ratio of terminal groups cannot be determined.

6.6 Conclusion

Catalytic chain transfer polymerisation has been shown to be an effective method for producing low molecular weight polymers of both NORBLOC and UVAM. While catalyst activity in the systems studied is somewhat lower than for more simple monomers such as MMA and styrene the functionality of both NORBLOC and UVAM has not been shown to have any adverse effect on the polymerisation system. The synthesis of random copolymers of HEMA / NORBLOC containing a polymerisable unsaturated bond has been shown to be a viable process. Copolymers of UVAM / HEMA synthesised by CCTP are likely to contain a significant proportion of internal unsaturated end groups. If these macromonomers were to be added to contact lens formulations for subsequent polymerisation the styrene terminal fraction would not be covalently incorporated into the polymer network. Subsequently additional processing steps would be required to remove the excess macromonomer from the contact lens. Evidence suggests that hydrogen atom donation from the Co(III)-H shows preference towards UVAM. By developing a feed system in which the polymerisations are starved of UVAM it may be possible to greatly reduce the quantity of internally unsaturated product. Production of block copolymers containing NORBLOC via the macromonomer approach seem to be unsuccessful however, using alternative methods of synthesis the block copolymer approach is still a viable option

for overcoming problems of compatibility in hydrophilic environments. Alternative methods of synthesis to consider are transition metal mediated living radical polymerisation and radical addition fragmentation transfer polymerisation (RAFT).

6.7 Additional Information

Copper mediated living radical polymerisation of both UVAM and NORBLOC has also been investigated. Several reactions were carried out with both monomers using standard TMM-LRP methodology at 90 °C. Due to the poor solubility of both monomers the reactions were carried out in a higher volume of solvent (90 % v/v) than typical (66 % v/v). Even after 48 hours no polymer was detected by either ^{1}H NMR or SEC analysis. Whilst the reason for this remains undetermined one possibility is that the monomers may co-ordinate to Cu via the three nitrogens. This would mean there was competition between monomer and ligand meaning there would be a lower level of active catalyst than predicted thus preventing initiation.

6.8 References

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Chapter 7

Experimental

7 Experimental

7.1 Analytical Techniques

7.1.1 Polymer Characterisation

In order to obtain information concerning composition, molecular weight and end functionality of polymers a variety of techniques have been used.

7.1.1.1 Nuclear Magnetic Resonance Spectroscopy

^{1}H and ^{13}C NMR spectra were obtained using a Bruker DPX300 or ACP400 spectrometer with a relaxation delay of five seconds for proton spectra.

Nuclear magnetic resonance (NMR) spectroscopy has been used to supply information regarding end group analysis and thus molecular weight through integration of the appropriate regions in the ^{1}H NMR spectra. It is also a useful tool for calculation of monomer conversion.

7.1.1.2 Size Exclusion Chromatography

Polymer molecular weight data was obtained through size exclusion chromatography using a Polymer Laboratories system equipped with two PL-gel 5μm mixed-C columns (300 × 7.5 mm) and a PL-gel 5μm guard column (50 × 7.5 mm). Injection was via a PL autoinjector. The system uses THF as the eluent at 1 mL min^{-1} driven by an ICI instruments LC 1110 dual piston HPLC pump. The system is fitted with both differential refractive index and ultra-violet detectors. Calibration was performed with

narrow molecular weight distribution PMMA standards (M_p = 200 to 157700) obtained from Polymer Laboratories and MMA dimer and trimer prepared by catalytic chain transfer polymerisation in our laboratories.

7.1.1.3 Gravimetry

For volatile monomers conversion data was obtained by drying a known mass of reaction mixture to constant weight by heating under vacuum at 60 °C.

7.1.2 Characterisation of Small Molecules

^{1}H and ^{13}C NMR spectra were recorded on Bruker ACF 250 or DPX300 spectrometers. Mass spectra were recorded using a Kratos MS80 and FTIR spectra were measured on a Bruker Vector 22 spectrometer fitted with a Golden Gate diamond attenuated total reflection (ATR) cell. Elemental analyses were performed with a Leeman Labs CE440 elemental analyser.

7.2 Polymerisation Procedure

The general procedures for polymerisations are outlined here and more specific examples are given subsequently. Schlenk tubes fitted with rubber septa or Viking caps or alternatively ampoules sealed with Rotaflow vacuum taps were used as reactors for the polymerisations. Schlenk line apparatus and standard techniques were employed to ensure all polymerisations were carried out under an inert atmosphere of nitrogen. Solid reagents were added to reactors before vacuum degassing / nitrogen purging three times. Liquid reagents were deoxygenated prior to use by purging with

nitrogen gas for in excess of one hour or alternatively by three consecutive freeze, pump, thaw cycles. The deoxygenated reagents were then transferred to the reactors via pre-dried, deoxygenated gas tight syringe. Typically reactions were then deoxygenated by three consecutive freeze, pump, thaw cycles before heating. The procedures outlined below for the different types of reactions are general procedures and any variation to these is discussed within the results and discussion section of the main texts.

7.2.1 Reagents and Suppliers

All materials were used as supplied unless otherwise stated. Solvents were used either as received or were purified by distillation under reduced pressure from calcium hydride and stored over 4 Å molecular sieves. All solvents were deoxygenated prior to use by purging with nitrogen for a minimum of 30 minutes. Methyl methacrylate, *n*-dodecyl methacrylate and n-butyl methacrylate were passed over a column of activated basic aluminium oxide to remove inhibitor then deoxygenated by purging with nitrogen and stored at 0 °C under nitrogen. 2,2'-Azobisisobutyonitrile was purified by three consecutive re-crystallisations from methanol. Tris(trimethylsiloxy)-3-methacryloxy propylsilane was distilled under reduced pressure to remove dimethacrylate and inhibitor, deoxygenated by four consecutive freeze, pump, thaw cycles and then stored at 0 °C under nitrogen. Ethyl 2-bromo-2-methylpropionate was deoxygenated by three consecutive freeze, pump, thaw cycles and stored under nitrogen.

Methanol (99 %), ethanol (99 %), anhydrous toluene (99.9 %), butan-1-ol (99.5 %), 2-butanone (99 %), 2,2'-azobisisobutyonitrile (97 %) (**BDH**): tris(trimethylsiloxy)-3-

methacryloxy propylsilane (TRIS) (minimum 75 %) (**Gelest**): ethyl 2-bromo-2-methylpropionate (98 %), 2-hydroxyethyl methacrylate (97 %), methyl methacrylate (99 %), 2-mercaptoethanol (98 %), mercaptoacetic acid (97 %), 4,4'-azobis(4-cyano-pentanoic acid) (CVA) (75+ %, remainder water), glycidyl methacrylate (97 %) (**Aldrich**): 2,2'-azobisisobutyrate (V-601), 2,2'-azobis [2-methyl-N-(2-hydroxyethyl) propionamide] (VA-086) (**WAKO):** 2-(2'-hydroxy-5'-methacrylyloxyethyl phenyl)-2H-benzotriazole (98 %) (**Noramco**): 2-(2-hydroxy-3-*tert*-butyl-5-vinylphenyl)-5-chloro-2H-benzotriazole (99.9 %) (**Organic Consultants**): 2-(methacryloxyethyl)-2'-(trimethylammoniumethyl)phosphate (98 %) (**Biocompatibles**).

7.2.2 Copper Mediated Living Radical Polymerisations

The method for a typical copper mediated living radical polymerisation is outlined below for MMA. Reactions with TRIS were deoxygenated more thoroughly and typically four or five consecutive freeze, pump, thaw cycles were carried out. Reactions were carried out in Schlenk tubes sealed with rubber septa or Viking caps. Cu(I)Br (0.134 g, 9.35 x 10^{-4} mol) was added to the reaction vessel which was then vacuum degassed / nitrogen purged three times. Toluene (20 mL), MMA (10 mL, 0.0935 mol) and *N*-(*n*-Propyl)-2-pyridylmethanimine (0.277 g, 1.87 × 10^{-3} mol) were then added by pre-dried gas tight syringe whilst stirring. Solutions were then deoxygenated by three consecutive freeze, pump, thaw cycles. The reactors were then placed into a pre-heated oil bath at 90 °C. After allowing five minutes for the solution to attain temperature ethyl 2-bromo-2-methylpropionate (0.137 mL, 9.33 × 10^{-4} mol) was added. Samples were taken using deoxygenated pipettes or deoxygenated gas tight syringe and immediately quenched by freezing in liquid nitrogen. Monomer

conversion was calculated through analysis of the ^{1}H NMR spectrum and molecular weight determined by SEC.

7.2.3 Catalytic Chain Transfer Polymerisations

Typically catalytic chain transfer polymerisations were carried out as described below for TRIS. CoBF (10 mg, 2.23×10^{-5} mol) was dissolved in 2-butanone (10 mL). This solution was then diluted by a factor 20 by taking 0.5 mL of the solution and adding 9.5 mL of 2-butanone to give a stock solution with a CoBF concentration of 1.12×10^{-3} M. This solution was then deoxygenated by four consecutive freeze, pump, thaw cycles. 2,2'-azobisisobutyonitrile (8.0 mg, 4.87×10^{-5} mol), tris(trimethylsiloxy)-3-methacryloxy propylsilane (5 mL, 1.09×10^{-2} mol) and CoBF stock solution (0.1 mL) were combined and the solution deoxygenated by four consecutive freeze, pump, thaw cycles. The reactor was then placed into a constant temperature water bath (60 °C, 48 hours). Monomer conversion was calculated through ^{1}H NMR spectra of the reaction solution. The polymer was then isolated by flash evaporation of solvent and removal of residual monomer under reduced pressure using Kugelrohr apparatus.

7.2.4 Catalytic Chain Transfer Polymerisations using a Feed System

Feed polymerisations were carried out by variations of the method described below, which is an example of production of 2-(methacryloxyethyl)-2'-(trimethylammoniumethyl)phosphate macromonomers.

Catalyst stock solution was prepared by dissolving CoBF (3.8 mg, 8.47×10^{-5} mol) in methanol (100 mL) with a concentration of 8.47×10^{-4} M and deoxygenating it with four consecutive freeze, pump, thaw cycles. A reactor solution of 4,4'-azobis(4-

cyano-pentanoic acid) (0.07 g, mol) and 2-(methacryloxyethyl)-2'-(trimethylammoniumethyl)phosphate (0.75 g, 2.54×10^{-3} mol) dissolved in water (25 mL) and methanol (7 mL) was prepared and subsequently CoBF stock solution was added (1 mL). A feed solution was prepared by dissolving 2-(methacryloxyethyl)-2'-(trimethylammoniumethyl)phosphate (5.0 g, 1.69×10^{-2} mol) in water (25 mL) and methanol (7.5 mL). CoBF stock solution (6.5 mL) was then added to this solution. The reactor was then placed into a constant temperature water bath (60 °C, 4hours) and the feed solution added over 90 minutes. After 2hours additional 4,4'-azobis(4-cyano-pentanoic acid) (0.035g, mol) was added. The reaction was quenched by cooling in liquid nitrogen. Monomer conversion was calculated through analysis of the ^{1}H NMR spectrum of the reaction solution and molecular weight information of dried samples calculated through ^{1}H NMR analysis and SEC where appropriate.

7.2.5 Determination of Catalyst Efficiencies (*Cs*)

Typically stock solutions of (i) initiator in monomer and solvent and (ii) CoBF in solvent/monomer were prepared and deoxygenated by four consecutive freeze, pump, thaw cycles. The required quantities of the stock solutions and additional solvent/monomer where required were placed into ampoules fitted with Youngs taps and deoxygenated by four consecutive freeze, pump, thaw cycles prior to heating in a constant temperature water bath (60 °C). Reactions were quenched at minimum conversion by cooling in liquid nitrogen. For each experiment five reactions were prepared consisting of four different [CoBF]/[Monomer] ratios (from identical stock solutions) and a control containing no catalyst.

The procedure is different for liquid and solid monomers and therefore examples are given below for the determination of the chain transfer constant to TRIS in 2-butanone and for NORBLOC in toluene.

TRIS: AIBN (0.0099 g, 6.03×10^{-5} mol) was dissolved in TRIS (6 mL, 0.102 mol) and 2-butanone (1 mL) and the solution deoxygenated by four consecutive freeze, pump, thaw cycles. CoBF (5.0 mg, 1.114×10^{-6} mol) was dissolved in 2-butanone (10 mL). This solution was then diluted by a factor 10 by taking 1 mL of the solution and adding 9 mL of 2-butanone to give a stock solution with a CoBF concentration of 1.114×10^{-4} M. Five solutions were then prepared, each containing 1 mL of the initiator solution and a further 0.5 mL made up from differing ratios of CoBF stock solution and 2-butanone. These five solutions were then deoxygenated by four consecutive freeze, pump, thaw cycles before being sealed and placed into a constant temperature water bath (60 °C, 45 mins). Monomer conversion and molecular weight analysis were determined from SEC of the reaction solutions without purification.

NORBLOC: The first stock solution is prepared by placing V-601 (0.012 g, 5.21×10^{-5} mol) and NORBLOC (6.0 g, 0.0186 mol) into a 50 mL volumetric flask and adding toluene to the mark. CoBF (3.90×10^{-3} g, 8.68×10^{-6} mol) is dissolved in toluene (100 mL). This solution was then diluted by a factor of 10 by taking 1 mL of the solution and adding 9 mL of toluene to give a stock solution of CoBF with a concentration of 8.68×10^{-6} M (3.90×10^{-6} g/mL, 8.68×10^{-9} mol/mL). Five solutions were then prepared, each containing 9 mL of the initiator / monomer solution and a further 0.16 mL made up from differing ratios of CoBF stock solution and toluene. These five solutions were then deoxygenated by four consecutive freeze, pump, thaw cycles before being sealed and placed into a constant temperature water bath (60 °C, 20

mins). Monomer conversion was calculated by ^{1}H NMR analysis and molecular weight analysis performed by SEC of the reaction solutions without purification.

7.2.6 Copolymerisations with Macromonomers

Copolymerisations of methacrylate monomers with macromonomers prepared by catalytic chain transfer were carried out in a similar procedure to that of copolymerisation of two monomers by conventional free radical polymerisation. An example of the copolymerisation of TRIS macromonomer with NORBLOC is outlined below.

In a typical polymerisation TRIS macromonomer (1.0 g, 5.26×10^{-4} mol), AIBN (0.013 g, 7.92×10^{-5} mol) and NORBLOC (2.3 g, 7.12×10^{-3} mol) were dissolved in toluene (30 mL). This solution was then deoxygenated by four consecutive freeze, pump, thaw cycles before heating in a constant temperature water bath (65 °C, 24 hours). The reaction was quenched by cooling in liquid nitrogen. Conversion and molecular weight data was obtained through analysis of the ^{1}H NMR spectrum of the reaction solution and by SEC.

7.2.7 Chain Transfer Polymerisations

In a typical polymerisation a mixture of tris(trimethylsiloxy)-3-methacryloxy propylsilane (46 mL, 0.118 mol), 2,2'-azobisisobutyonitrile (0.20 g, 1.22×10^{-3} mol) and 2-mercaptoethanol (2.53 mL, 0.036 mol) was deoxygenated by purging with nitrogen for 30 minutes. The mixture was then heated (60 °C, 72 hours) under a nitrogen blanket. The solution was then cooled and poured into diethyl ether (250 mL). The solution was then washed with water (3 × 250 mL) and subsequently the

organic layer was dried with magnesium sulphate. The solution was filtered and the polymer isolated by rotary evaporation of the solvent. Monomer conversion was calculated through ^{1}H NMR analysis and molecular weight information obtained from SEC.

7.3 Synthesis of Bis(boron difluorodimethylgloximate) cobaltate(II) (CoBF)

7.3.1 Reagents and Suppliers

Cobalt(II) acetate tetrahydrate (98 %), boron trifluoride etherate (purified, redistilled) (**Aldrich**): Dimethyl glyoxime (99 %) (**Lancaster**): methanol (99.5 %), ethyl acetate (99.5 %) (**BDH**): sodium hydrogen carbonate (99.5 %) (**Philip Harris**). All materials were used as supplied unless otherwise stated. All solvents were deoxygenated prior to use by purging with nitrogen for a minimum of 30 minutes.

7.3.2 Synthesis

CoBF was prepared by a modification of a synthesis developed by Zeneca, a nitrogen atmosphere was maintained throughout the preparation, purification and isolation and all solvents were deoxygenated prior to use. Cobalt (II) acetate tetrahydrate was dried by placing under vacuum and heating for 72 hours. The dried dark purple cobalt salt (12.2 g, 0.075 mol) and dimethyl glyoxime (17.4 g, 0.150 mol) were placed into the reactor and vacuum degassed / nitrogen purged four times. Subsequently ethyl acetate (300 mL), previously deoxygenated by purging with nitrogen for 60 minutes, was added to the reactor and vigorously stirred. Immediately boron trifluoride etherate

(50.7 mL, 0.413 mol) was added dropwise over 10 minutes. The reaction mixture became a deep orange colour before addition was complete. The solution was warmed (50 °C, 20 mins) and then cooled, using an ice bath, to room temperature. Sodium hydrogen carbonate (13.9 g) was then slowly added to the reaction mixture to avoid excess effervescence. The product was then crystallised by cooling (~10 °C) for one hour whilst continually stirring. The solution was then removed from the reaction mixture using a cannular fitted with a filter paper. Using this filtration method the product was washed with distilled water (3 × 100 mL) and subsequently methanol (3 × 100 mL). The product was then dried by warming (40 °C) under vacuum. The deep red/brown product was then dissolved in ethyl acetate and a small amount of grey insoluble material was removed by filtration. The ethyl acetate was then removed by flash evaporation and the solid product slurried with methanol (100 mL) then filtered and dried under vacuum (40 °C). The dark red/brown crystals of CoBF were obtained in 38 % yield (12.7 g). IR ν (cm^{-1}); 825, 945, 1090, 1160, 1620. UV-visible (methanol, nm); 270, 330, 460. Elemental Analysis for the bis(methanol) adduct, $CoC_{10}H_{20}N_4O_6B_2F_4$: calculated C 26.76, H 4.49, N 12.48; experimental C 25.93, H 4.68, N 12.76.

7.4 Purification of Copper (I) Bromide

7.4.1 Reagents and Suppliers

Copper (I) bromide (98 %) (**Avocado**): Glacial acetic acid (99 %), absolute ethanol (99 %), anyhdrous diethyl ether (98 %) (**BDH**): Sodium Sulfite (98 %), sulphuric acid (95-98 %) (**Aldrich**). All materials were used as supplied unless otherwise stated.

7.4.2 Procedure

Copper (I) bromide was purified by a modification of the method outlined by Keller and Wycoff [1]. Using a pestle and mortar Copper (I) bromide (50 g, 0.35 mol) was ground to a fine powder. Using dilute sulphuric acid (15 mL, 2 M) the fine copper powder was turned into a green paste. The paste was filtered under a blanket of nitrogen and the copper(I) bromide was washed with glacial acetic acid (250 mL), absolute ethanol (250 mL) and anhydrous diethyl ether (250 mL). The powder was then dried in a vacuum oven (12 hours, 150 °C). The off white Cu(I)Br powder was obtained in 74.4 % yield (37.2 g).

7.5 Synthesis of *N*-(*n*-Alkyl)-2-pyridylmethanimine Ligands

A series of these Schiff base compounds were prepared by a modification of the Baehr and Doege method[2].

7.5.1 Reagents and Suppliers

Pyridine-2carboxaldehyde (99 %) (**Avocado**): *n*-propylamine (99 %) (**Aldrich**): *n*-octylamine (98 %) (**Lancaster**): diethyl ether (98 %) (**BDH**): magnesium sulphate, dried (99.5 %) (**Philip Harris**). All reagents were used as supplied unless otherwise stated.

7.5.2 Synthesis of *N*-(*n*-Propyl)-2-pyridylmethanimine

Pyridine-2-carboxaldehyde (40 mL, 0.42 mol) was dissolved in diethyl ether (20 mL) and cooled in an ice bath. Whilst stirring *n*-propylamine (40 mL, 0.53 mol) was added dropwise. On complete addition of the amine dried magnesium sulphate (10 g) was added and the slurry stirred (2 hours, 25 °C). The solution was then filtered and the solvent removed on a rotary evaporator. The product was purified by distillation under reduced pressure (0.005 mmHg, 43 °C) to give a pale yellow oil. The product was obtained in 92.1 % yield (57.3 g).

^{1}H NMR ($CDCl_3$, 298 K, 300 MHz): δ 8.62 (d, 1H), 8.36 (s, 1H), 7.98 (d, 1H), 7.68 (t, 1H), 7.27 (t, 1H), 3.61 (t, 2H), 1.73 (sextet, 2H), 0.91 (t, 3H). ^{13}C NMR ($CDCl_3$, 298 K, 300 MHz): δ 161.2, 154.3, 149.0, 136.1, 124.1, 120.8, 62.9, 23.7, 11.6. IR ν (cm^{-1}); 3050, 3010 (Ar C-H str.), 2960-2840 (Alkyl C-H str.), 1650 (C=N str.), 1590, 1570, 1470, 1430 (Ar ring str.). m/z +1 =149 Da. Elemental Analysis, $C_9H_{12}N_2$: calculated C 72.9, H 8.2, N 18.9; experimental C 71.4, H 8.1, N 18.6.

7.5.3 Synthesis of *N*-(*n*-Pentyl)-2-pyridylmethanimine

Preparation as for N-(*n*-propyl)-2-pyridylmethanimine except *n*-pentylamine (45 mL, 0.39 mol) and pyridine-2-carboxaldehyde (30 mL, 0.32 mol) were used. The product was distilled under reduced pressure (0.04 mmHg, 60 °C). The product was obtained in a 91.1 % yield (51.6 g).

^{1}H NMR ($CDCl_3$, 298 K, 300 MHz): δ 8.62 (d, 1H), 8.36 (s, 1H), 7.98 (d, 1H), 7.68 (t, 1H), 7.27 (t, 1H), 3.61 (t, 2H), 1.73 (quintet, 2H), 1.34 (m, 4H), 0.91 (t, 3H). ^{13}C NMR ($CDCl_3$, 298 K, 300 MHz): δ 161.3, 154.4, 149.7, 136.1, 124.2, 120.8, 61.2,

30.1, 29.2, 22.2, 13.7. IR ν (cm^{-1}); 3050, 3010 (Ar C-H str.), 2970-2850 (Alkyl C-H str.), 1650 (C=N str.), 1590, 1570, 1470, 1440 (Ar ring str.). m/z +1 =177 Da. Elemental Analysis, $C_{11}H_{16}N_2$: calculated C 74.9, H 9.2, N 15.9; experimental C 74.3, H 9.2, N 15.7.

7.5.4 Synthesis of *N*-(*n*-Octyl)-2-pyridylmethanimine

Preparation as for N-(*n*-propyl)-2-pyridylmethanime except *n*-octylamine (50 mL, 0.30 mol) and pyridine-2-carboxaldehyde (20 mL, 0.21 mol) were used. The product was distilled under reduced pressure (0.03 mmHg, 101 °C). The product was obtained in a 90.9 % yield (41.8 g).

^{1}H NMR ($CDCl_3$, 298 K, 300 MHz): δ 8.62 (d, 1H), 8.36 (s, 1H), 7.98 (d, 1H), 7.68 (t, 1H), 7.27 (t, 1H), 3.61 (t, 2H), 1.73 (quintet, 2H), 1.27 (m, 10H), 0.83 (t, 3H). ^{13}C NMR ($CDCl_3$, 298 K, 300 MHz): δ 161.2, 154.3, 149.0, 136.1, 124.1, 120.8, 62.9, 31.8, 30.6, 29.3, 29.2, 27.2, 22.5, 14.0. IR ν (cm^{-1}); 3050, 3010 (Ar C-H str.), 2950-2860 (Alkyl C-H str.), 1650 (C=N str.), 1590, 1570, 1470, 1440 (Ar ring str.). m/z +1 =219 Da. Elemental Analysis, $C_{14}H_{22}N_2$: calculated C 77.0, H 10.2, N 12.8; experimental C 76.5, H 10.1, N 13.1.

7.6 Preparation of Initiators for TMM-LRP

7.6.1 Reagents and Suppliers

Anhydrous tetrahydrofuran (99.9 %), triethylamine (> 99 %), dichloromethane (99.0%), sodium hydrogen carbonate (99:5 %) sodium hydroxide (> 99 %), hydrochloric acid (35-38 %) (**BDH**): 2-bromoisobutyryl bromide (98 %), anhydrous ethylene glycol (99.8 %), 2-propen-1-ol (99 %), 4-(dimethylamino)pyridine (97 %), polyethylene glycol (*Mn ca.*1500) (**Aldrich**): anyhdrous magnesium sulphate (99.5 %) (**Fisons**). All reagents were used as received unless otherwise stated. Triethylamine was dried by storing over potassium hydroxide for a minimum of 12 hours prior to use.

7.6.2 Synthesis of Poly(ethylene glycol) di(2'-methyl-2'-bromopropionate)

Poly(ethylene glycol) (*Mn ca.* 1500, 40 g, 2.66×10^{-2} mol) was dissolved in a mixture of anhydrous tetrahydrofuran (200 mL) and triethylamine (9 mL, 6.46×10^{-2} mol). To this solution 2-bromoisobutyryl bromide (13.4 g, 0.058 mol) was added dropwise whilst vigorously stirring. The solution was left for 24 hours before washing with saturated sodium hydrogen carbonate solution (4 × 300 mL). The organic phase was then filtered. Then the solvent was removed from the filtrate by rotary evaporation.

^{1}H NMR ($CDCl_3$, 298 K, 300 MHz): δ 4.23 (t, 4H, $CO_2C\underline{H}_2$), 3.25-3.8 ($OC\underline{H}_2$), 1.84 (s, 6H, $C(C\underline{H}_3)_2Br$.^{13}C NMR ($CDCl_3$, 298 K, 300 MHz): δ 70.9, 69.0, 65.4, 31.1. IR ν (cm^{-1}); 3000-2760 (C-H str. Broad), 1730 (C=O str.).

7.6.3 Synthesis of 2-Hydroxyethyl-2'-methyl-2'-bromopropionate

2-Hydroxyethyl-2'-methyl-2'-bromopropionate was prepared by a variation of the method described by Haddleton *et al.*[3]. Anhydrous ethylene glycol (1 L, 17.9 mol) and triethylamine (100 mL, 0.72 mol) were placed into a flask under an dry atmosphere of nitrogen and stirred vigorously. To this flask a solution of 2-Bromoisobutyryl bromide (20 mL, 0.16 mol) in anhydrous tetrahydrofuran (500 mL) was added dropwise over 5 hours. The solution was then heated (50 °C) for 2 hours before filtering. Portions of the solution (~500 mL) were then poured into water (500 mL) and the product extracted into chloroform (3 × 100 mL). The chlorofrom fractions were then combined and reduced by rotary evaporation of the solvent (to ~500 mL) before being washed with sodium hydrogen carbonate solution (2 × 250 mL). The solution was then dried with magnesium sulphate, filtered and the solvent removed on a rotary evaporator. The clear liquid product was then isolated by distillation under reduced pressure (65 °C, 0.1 mmHg) in a 15.3 % yield (5.2 g).

^{1}H NMR ($CDCl_3$, 298 K, 300 MHz): δ 4.30 (t, 2H), 3.85 (t, 2H), 1.94 (s, 6H). ^{13}C NMR ($CDCl_3$, 298 K, 300 MHz): δ 171.83, 67.30, 60.70, 55.72, 30.59. IR ν (cm^{-1}); 3350 (O-H str. broad), 3020-2810 (C-H str.), 1730 (C=O str.). m/z +1 = 211 Da. Elemental Analysis, $C_6H_{11}BrO_3$: calculated C 34.16 H 5.21; experimental C 33.78, H 5.29.

7.6.4 Synthesis of Allyl 2-bromo-2-methylpropionate

Allyl 2-bromo-2-methylpropionate was synthesised by a modification of the method of . A solution of 2-propen-1-ol (12 mL, 0.18 mol), triethylamine (100 mL, 0.72 mol),

4-(dimethylamino)pyridine (0.04 g, $3.2x10^{-4}$ mol) and anhydrous tetrahydrofuran (100 mL) was cooled using an ice bath (0 °C). The solution was stirred vigorously and 2-bromoisobutyryl bromide (20 mL, 0.16 mol) was added dropwise over 4 hours. On complete addition the solution was left to stand for a further two hours before being dropped into ice cold water (500 mL). The product was extracted into dichloromethane (500 mL) and then washed with water (500 mL), 10% hydrochloric acid / water (250 mL) and saturated sodium hydrogen carbonate solution. Subsequently the solvent was removed using a rotary evaporator before distillation under static vacuum (45 °C) to yield a clear colourless liquid (23.44 g, 70.6 %)

^{1}H NMR ($CDCl_3$, 298 K, 300 MHz): δ 5.95-5.82 (m, 1H), 5.36 & 5.23 (dq, 1H), 5.30 & 5.20 (dq, 1H), 4.62 & 4.60 (dt, 2H), 1.89 (s, 6H). ^{13}C NMR ($CDCl_3$, 298 K, 300 MHz): δ 171.62, 131.80, 118.87, 66.78, 56.01, 31.14. IR ν (cm^{-1}); 3090 (alkene C-H str.), 3040-2830 (C-H str. Broad), 1730 (C=O str.), 1650 (C=C str.), 1460 (alkene C-H bend). m/z +1 = 208 Da. Elemental Analysis, $C_7H_{11}BrO_2$: calculated C 40.60, H 5.31; experimental C 40.63, H 5.21.

7.7 Preparation of Silyl Enol Ethers

7.7.1 Reagents and Suppliers

4'-Hydroxyacetophenone (99 %), chlorotrimethylsilane (98 %), 4'-benzyloxyacetophenone (98 %) (**Aldrich**): tetrahydrofuran (99.5 %), anhydrous pentane (99.9 %) (**BDH**): lithium diisopropyl amide (2.0 M soln. in THF/hexane) (**Acros**).

7.7.2 Synthesis of Trimethyl(1-(trimethylsiloxy)phenylethenyloxy)silane

4'-Hydroxyacetophenone (30 g, 0.22 mol) was dissolved in THF (450 mL) and subsequently cooled to –78 °C. 2.4 molar equivalents of lithium diisopropyl amide (270 mL of 2.0 M in THF/hexane, 0.54 mol) was then added dropwise whilst vigorously stirring. This mixture was then stirred for a further 2 hours prior to the dropwise addition of chlorotrimethylsilane (70 mL, 0.55 mol). On completion of addition the solution was allowed to warm to room temperature (2 hours) before passing over celite and removing the solvents *in vacuo*. The product was dissolved in anhydrous pentane and passed over celite again. The pentane was removed *in vacuo* to yield the crude product. The product was obtained in its pure form by distillation from trap to trap under reduced pressure.

^{1}H NMR ($CDCl_3$, 298 K, 300 MHz): δ 7.53 (d, 2H, J 8.85 Hz), 6.84 (d, 2H, J 8.85), 4.84 (s, 1H), 4.38 (s, 1H), 0.31 (s, 18H). ^{13}C NMR ($CDCl_3$, 298 K, 300 MHz): δ 155.8, 131.0, 128.2, 126.7, 119.8, 90.0, 0.3. IR ν (cm^{-1}); 3040 (broad) (alkene & Ar. C-H str.), 2960, 2900 (Me asym. & sym. str.), 1610 (broad), 1510 (Alkene and Ar. ring str.), 1430 (alkene C-H bend). m/z +1 = 281 Da. Elemental Analysis, $C_{14}H_{24}O_2Si_2$: calculated C 59.94, H 8.62; experimental C 59.89, H 8.76.

7.7.3 Synthesis of Trimethyl(*p*-(benzyloxy)phenylethenyloxy)silane

The synthesis was carried out identically to that of trimethyl(1-(trimethylsiloxy)phenylethenyloxy)silane except for the following changes. 4'-benzyloxyacetophenone (20 g, 0.088 mol), LDA (45 mL, 2.0 M in THF/hexane,

0.090 mol) and chlorotrimethylsilane (13 mL, 0.102 mol) were used. NMR spectra of the crude product showed it contained a small quantity of unreacted starting material, however as this would not effect the compounds desired use no further purification was required.

^{1}H NMR ($CDCl_3$, 298 K, 300 MHz): δ 7.41 (d, 2H, J 8.85 Hz), 7.35-7.05 (m, 5H), 6.80 (d, 2H, J 8.89), 4.93 (s, 2H), 4.68 (s, 1H), 4.22 (s, 1H), 0.15 (s, 18H).^{13}C NMR ($CDCl_3$, 298 K, 300 MHz): δ 155.8, 131.0, 128.2, 126.7, 119.8, 89.3, 0.1. IR ν (cm^{-1}); 3050-3020 (alkene & Ar. C-H str.), 3000-2860 (C-H str.), 1610 (broad), 1510, 1450 (Alkene and Ar. ring str.), 1430 (alkene C-H bend). m/z = 298 Da.

7.8 Reactions of Tertiary Bromide Terminated PMMA

A sample of PMMA was prepared by TMM-LRP as outlined in *section 7.2.2* Reactions of the tertiary bromide end group of this polymer were carried out under standard TMM-LRP conditions in the absence of oxygen.

7.8.1 Reagents and Suppliers

TEMPO (98 %), Cu Powder (99 %), $Cu(II)Br_2$ (99 %), allyl bromide (97 %), maleic anhydride, briquettes (99 %), ethylene (99.5 %), divinylbenzene (mixture of isomers) (**Aldrich**): benzyl acrylate (97 %) (**Lancaster**): toluene (99 %) (**BDH**).

7.8.2 Reaction of PMMA from TMM-LRP with TEMPO

TEMPO (1.42 g, 9.09×10^{-3} mol), Cu(I)Br (0.132 g, 9.20×10^{-4} mol), *N*-(*n*-propyl)-2-pyridylmethanimine (0.28 mL, 1.99×10^{-3} mol) and ω-bromo PMMA (3.0 g) in

toluene (10 mL) were stirred at 90 °C for 3 hours. ^{1}H NMR ($CDCl_3$, 323 K, 400 MHz; specific resonances) δ 6.16-6.22 (s, 1H, HHC=, I=15.17373), 5.43-5.54 (m, 1H, HHC=, I=16.15609), 4.00-4.25 (m, 2H, α-OCH_2CH_3, I=39.99231), 3.70-3.75 (s, 3H, ω-OCH_3), 3.35-3.85 (s, 3nH, OCH_3), 2.42-2.71 (m, 2H, ω-CH_2 backbone, I=30.97464). Yield = 77.9%.

7.8.3 Reaction of PMMA from TMM-LRP with Trimethyl(1-(trimethylsiloxy)phenylethenyloxy)silane

Trimethyl(1-(trimethylsiloxy)phenylethenyloxy)silane (2.25 g, 8.04 × 10^{-3} mol), Cu(I)Br (0.132 g, 9.20 × 10^{-4} mol), *N*-(*n*-propyl)-2-pyridylmethanimine (0.28 mL, 1.99 × 10^{-3} mol) and ω-bromo PMMA (3.0 g) in toluene (10 mL) were stirred at 90 °C for 3 hours. ^{1}H NMR (d_6-DMSO, 323 K, 400 MHz; specific resonances) δ 9.45 (s, 1H, OH), 7.75-7.85 and 6.80-6.90(each d, 2H, Ph), 4.01-4.12 (m, 2H, α-OCH_2CH_3). Yield *ca.* 100%.

7.8.4 Reaction of PMMA from TMM-LRP with Allyl Bromide

Copper powder (0.30 g, 4.72 × 10^{-3} mol), Cu(I)Br (0.1316 g, 9.17 × 10^{-4} mol), *N*-(*n*-propyl)-2-pyridylmethanimine (0.28 mL, 1.99 × 10^{-3} mol) and ω-bromo PMMA (3.0 g) in toluene (10 mL) and allyl bromide (8 mL, 4.73 × 10^{-2} mol) were stirred at 50 °C for 24 hours. ^{1}H NMR ($CDCl_3$, 323 K, 400 MHz; specific resonances) δ 5.42-5.72 (m, 1H, H_2C=CH-, I=2.53125), 4.84-5.06 (m, 2H, H_2C=CH-, I=4.53181), 3.93-4.13 (m, 2H, α-OCH_2CH_3, I=8.23105), 3.35-3.90 (s, 3nH, OCH_3). Yield = 57.2%.

7.8.5 Reaction of PMMA from TMM-LRP with Divinylbenzene

Cu(I)Br (0.132 g, 9.20×10^{-4} mol), *N*-(*n*-octyl)-2-pyridylmethanimine (0.42 mL, 2.99×10^{-3} mol) and ω-bromo PMMA (3.0 g) in toluene (20 mL) and divinylbenzene (13 mL, 0.109 mol) were stirred at 25 °C for 24 hours. ^{1}H NMR (d_6-DMSO, 323 K, 400 MHz; specific resonances) δ 6.91-7.60 (m, 4H, Ph) and 6.61-6.86 (m, 1H, H_2C=C<u>H</u>-) total I=2.5094, 5.68-5.95 (m, 1H, <u>H</u>HC=CH-), 5.10-5.39 (m, 1H, H<u>H</u>C=CH-; I=0.5180), 4.00-4.14 (m, 2H, α-OC<u>H</u>$_2$CH$_3$, I=1.000). Yield *ca.* 100%.

7.8.6 Reaction of PMMA from TMM-LRP with Benzyl Acrylate

Cu(I)Br (0.132g, 9.20×10^{-4} mol), *N*-(*n*-octyl)-2-pyridylmethanimine (0.42 mL, 2.99×10^{-3} mol) and ω-bromo PMMA (3.0 g) in toluene (20 mL) and benzyl acrylate (14 mL, mol) were heated at 25 °C for 24 hours. Experiment 2 as Experiment 1 with 1.4 mL benzyl acrylate; Experiment 3 as Experiment 1 with 0.100 g of Cu(I)Br and 0.0442 g of Cu(II)Br$_2$ for 4 hours at 60 °C; Experiment 4 as Experiment 1 with 0.065 g of Cu(I)Br and 0.1005 g of Cu(II)Br$_2$ for 4 hours at 60 °C. ^{1}H NMR ($CDCl_3$, 323 K, 400 MHz; specific resonances) δ 7.06-7.41 (m, 5H, Ph), 5.05-5.20 (s, 2H, benzylic) 4.14-4.34 (m, 1H, ω-C<u>H</u>Br), 3.93-4.13 (m, 2H, α-OC<u>H</u>$_2$CH$_3$, I=1.000). Yield exp.1 = 66.6%; exp.2 = 56.9%; exp.3 = 62.3%; exp.4 = 23.4%.

7.8.7 Reaction of PMMA from TMM-LRP with Ethylene

Cu(I)Br (0.132 g, 9.20×10^{-4} mol), *N*-(*n*-octyl)-2-pyridylmethanimine (0.42 mL, 2.99×10^{-3} mol) and ω-bromo PMMA (3.0 g) in toluene (20 mL) were heated and stirred at 90 °C while purging with ethylene gas for 45 mins. Yield *ca.* 100% based on

the complete disappearance of both the ω-OCH_3 and the C-Br resonances of the starting PMMA. ^{13} C-NMR ($CDCl_3$, 323 K; specific resonances) δ 30.2 and 30.4 (CH_2Br) 29.6-29.8 (CH_2CH_2Br).

7.8.8 Reaction of PMMA from TMM-LRP with Maleic Anhydride

Maleic anyhydride (1.78 g, 1.82×10^{-2} mol), Cu(I)Br (0.13 g, 9.06×10^{-4} mol), *N*-(*n*-propyl)-2-pyridylmethanimine (0.28 mL, 1.99×10^{-3} mol) and ω-bromo PMMA (3.0 g)in toluene (20 mL) were stirred at 90 °C for 4 hours. Yield *ca.* 100% (^{1}H NMR analysis) FT-IR (specific): carbonyl stretching of the anhydride at 1781 cm^{-1}.

7.9 References

1 R. N. Keller and H. D. Wycoff, *Inorg. Synth.*, 1947, **2**.

2 Baehr and Doege, *Z. Anorg. Allg. Chem.*, 1957, **292**, 119.

3 D. M. Haddleton, C. Waterson, P. J. Derrick, C. Jasieczek and A. J. Shooter, *Chem. Commun.*, 1997, **7**, 683.

Chapter 8

Appendix

8 Appendix

8.1 Additional Data for *Chapter 3*

Data for *figures 3.18 & 3.19*

	Time (mins)	Conversion (%)	ln $[M]_0/[M]$	*Mn* (theory)	*Mn* (SEC)	PDI
	15	14.3	0.154	910	2090	1.26
	30	24.1	0.276	1400	2820	1.17
	45	32.7	0.396	1830	3070	1.21
Control	65	41.1	0.522	2310	3300	1.21
	90	47.6	0.619	2510	3790	1.19
	120	56.0	0.822	3000	4300	1.16
	180	67.0	1.107	3550	4590	1.182
	240	74.9	1.380	3940	4990	1.191
A	90	48.6	0.665	2630	3160	1.19
	240	51.5	0.724	3030	2830	1.36
B	90	49.6	0.685	2680	3120	1.20
	240	53.6	0.767	3230	2820	1.36

8.2 Additional Data for *Chapter 4*

Data for *figures 4.12-4.22*

	Time (mins)	Conversion (%)	ln $[M]_0/[M]$	*Mn* (theory)	*Mn* (SEC)	PDI
	30	31.3	0.375	7980	8280	1.14
	60	39.3	0.500	10030	10530	1.10
	120	51.9	0.732	13230	12780	1.11
A1	180	55.3	0.805	14100	13720	1.11
	240	59.2	0.896	15090	14100	1.11
	300	61.3	0.950	15640	13610	1.13
	360	63.7	1.013	16240	14240	1.12

	30	22.0	0.249	5620	7170	1.15
	60	38.1	0.480	9720	10040	1.11
	120	49.2	0.678	12550	13310	1.10
A2	180	52.5	0.745	13400	13740	1.12
	240	54.7	0.791	13930	13680	1.14
	300	55.6	0.812	14170	14680	1.09
	360	58.5	0.879	14910	15030	1.10
	30	24.7	0.283	6290	4850	1.50
	60	26.5	0.308	6750	6630	1.15
	120	30.2	0.360	7700	8570	1.10
A3	180	34.4	0.421	8770	8910	1.09
	240	36.0	0.446	9170	8810	1.12
	300	37.3	0.466	9500	8780	1.15
	360	37.5	0.470	9570	9370	1.10
	30	21.8	0.246	9230	4600	1.59
	60	24.5	0.281	10340	8860	1.66
	120	40.7	0.523	17210	10930	1.46
B1	180	54.4	0.785	22990	11540	1.37
	240	65.1	1.052	27520	14080	1.39
	300	72.0	1.272	30430	19820	1.16
	360	78.4	1.533	33150	20480	1.18
	1320	93.6	2.748	39570	25320	1.26
	30	5.8	0.059	2430	4420	1.14
	60	12.3	0.131	5210	5820	1.12
B2	120	21.9	0.247	9270	7420	1.12
	180	27.8	0.326	11750	8570	1.13
	240	34.2	0.418	14440	10000	1.12
	300	39.8	0.507	16820	11200	1.11
	360	42.3	0.549	17870	12360	1.11
	420	50.3	0.699	21270	13100	1.11

	30	14.7	0.159	6230	7750	1.18
	60	24.5	0.282	10380	9970	1.15
	120	33.3	0.404	14060	14090	1.13
B3	180	46.0	0.617	19460	17830	1.13
	240	54.1	0.778	22860	20250	1.13
	300	56.6	0.835	23940	22440	1.15
	360	62.4	0.978	26380	24310	1.15
	1320	92.5	2.596	39130	34690	1.36
	30	10.2	0.107	4300	4260	1.55
	60	16.6	0.181	7010	5110	1.47
	120	23.3	0.266	9870	7130	1.43
B4	180	33.1	0.402	13990	9980	1.44
	240	-	-	-	-	-
	300	45.4	0.604	19180	13360	1.39
	360	57.3	0.851	24230	14760	1.36
	1320	95.3	3.052	40280	26740	1.26
	30	57.9	0.866	6120	5640	1.61
	60	74.9	1.381	7910	7390	1.31
	120	86.6	2.007	9150	8610	1.27
C1	180	91.5	2.468	9670	8480	1.27
	240	94.5	2.904	9990	8600	1.27
	300	93.4	2.716	9870	8710	1.28
	1320	94.0	2.808	9930	8730	1.31
	30	31.0	0.370	3270	2280	1.42
	60	39.0	0.494	4120	2890	1.37
	120	56.5	0.833	5980	4390	1.39
C2	180	69.5	1.187	7340	5920	1.35
	240	76.5	1.449	8090	6280	1.26
	300	80.1	1.613	8460	6500	1.31
	360	84.1	1.839	8890	7260	1.17
	1320	95.5	3.093	10090	7420	1.21

	30	31.9	0.385	890	2880	1.13
	60	47.7	0.648	1220	3230	1.14
	90	63.8	1.017	1560	3420	1.14
D1	120	69.0	1.171	1670	3450	1.15
	180	79.0	1.561	1880	3600	1.13
	240	84.2	1.846	1990	3700	1.13
	300	86.2	1.979	2030	3700	1.14
	30	36.8	0.458	990	2650	1.12
	60	51.3	0.720	1300	3040	1.13
	90	64.3	1.031	1570	3210	1.13
D2	120	65.6	1.066	1600	3300	1.13
	180	75.6	1.411	1810	3380	1.13
	240	81.9	1.709	1940	3450	1.13
	300	84.2	1.846	1990	3510	1.14
	30	21.2	0.238	740	3440	1.39
	60	34.0	0.415	1070	3410	1.21
	90	49.0	0.674	1450	3770	1.16
E1	120	56.2	0.827	1630	3880	1.17
	180	72.4	1.288	2040	3980	1.18
	240	80.4	1.630	2240	4150	1.17
	300	81.7	1.696	2280	4240	1.18
	360	88.4	2.155	2450	4210	1.17
	30	17.2	0.189	640	2410	1.11
	60	-	-	-	2880	1.13
	90	51.2	0.717	1500	3230	1.13
E2	120	61.1	0.944	1750	3460	1.13
	180	70.1	1.207	1980	3630	1.14
	240	75.3	1.398	2110	3710	1.13
	300	81.0	1.658	2260	3770	1.14

8.3 Additional Data for *Chapter 5*

Data for *figure 5.8*

	Time (mins)	Conversion (%)	ln $[M]_0/[M]$	*Mn* (theory)
	10.25	28.4	0.334	1420
	15.75	35.1	0.433	1760
	21.25	43.7	0.575	2190
	26.75	47.8	0.651	2390
	32.25	53.9	0.774	2690
	37.75	58.2	0.873	2910
	48.75	66.5	1.094	3330
D3	59.75	71.4	1.251	3570
	70.75	76.1	1.430	3800
	81.75	79.2	1.572	3960
	92.75	82.8	1.763	4140
	103.75	85.8	1.955	4290
	114.75	87.0	2.038	4350
	120.25	90.2	2.322	4510
	5.25	59.3	0.898	2960
	10.75	76.1	1.430	3800
	16.25	81.5	1.690	4080
	21.75	84.9	1.889	4240
D4	27.25	87.3	2.066	4370
	32.75	89.5	2.250	4470
	38.25	90.2	2.323	4510
	43.75	91.5	2.469	4580
	49.25	92.3	2.559	4610
	54.75	93.0	2.663	4650

DX

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